

Table 8.11-1

Immunomodulators that Have Been Used in Horses

Source	Product	Dose	Frequency*	Route
Bacterial extracts	<i>Propionibacterium acnes</i> (EqStim ^a)	1 ml/114 kg	q48-72h	IV
	<i>Mycobacterium</i> spp. (Equimmune IV ^b)	1.5 ml/horse	q1-3w	IV
Virus products	Parapoxvirus ovis (Baypamun HK ^c)	2 ml/horse	q48h	IM
Serum products	Caprine Serum (Caprine Serum Fraction ^d)	2 ml/horse	q7-10d	IM
Cytokines	Interferon- α -2a (Roferon-A ^e)	0.1 U/kg	q24h, 5 days	PO
Synthetic products	Levamisole (Levasole, ^f Ripercol L ^g)	2 mg/kg	q48h	PO

q48-72h, Every 48 to 72 hours; q1-3w, every 1 to 3 weeks; q7-10d, every 7 to 10 days; IV, intravenous; IM, intramuscular; PO, by mouth.

*See text for details.

^aImmunovet, Neogen Co., Lansing, Mich.

^bVetrepharm Research Inc., Athens, Ga.

^cBayer AG, Leverkusen, Germany.

^dCentaur, Inc., Overland Park, Kan.

^eRoche Laboratories, Inc., Nutley, N.J.

^fSchering-Plough Animal Health Co., Union, N.J.

^gAmerican Cyanamid, Parsippany, N.J.

BOX 8.11-1

In Vitro Immunologic Testing Used to Characterize Immunodeficiencies and Immunomodulatory Differences

Total and differential white cell counts in peripheral blood
 Total and differential white cell counts in BALF
 Serum immunoglobulin isotypes, concentrations, and electrophoresis
 Mucosal immunoglobulin isotypes and concentrations
 Lymphocyte subpopulation phenotyping
 Mitogen lymphoproliferation
 Cytokine production
 Phagocytosis and oxidative burst activity
 CTL and LAK cell responses
 NK cell activation

BALF, Bronchoalveolar lavage fluid; CTL, cytotoxic lymphocyte; LAK, lymphocyte-activated killer; NK, natural killer.

PROPIONIBACTERIUM ACNES

Inactivated *Propionibacterium acnes*, formerly known as *Corynebacterium parvum*, has demonstrated immunostimulatory activity in *in vitro* and *in vivo* studies in the last 40 years, including macrophage activation, enhanced natural killer (NK) cell activity, increased CD8⁺ T lymphocyte expression with interferon release, inhibition of tumor growth, and nonspecific resistance to pathogenic challenge in mice, human patients, and domestic animals.

EqStim (Immunovet, Neogen Co., Lansing, Mich.) is licensed by the United States Department of Agriculture (USDA) as a biologic response modifier for adjunct therapy in the treatment of primary and secondary viral and bacterial infections of the respiratory tract of the horse in

association with other conventional therapy. It contains 0.4 mg/ml of nonviable *P. acnes* in a 12.5% ethanol-in-saline solution. The recommended dose is 1 ml per 114 kg of body weight, intravenously, two to three doses every 48 or 72 hours, before stress is induced or as an adjunct to conventional therapy. Mild fever after administration of the product is expected and indicates immune response.

In healthy young horses, a series of three intravenous injections of *P. acnes* results in immunomodulatory responses. In the peripheral blood, total and proportional CD4⁺ T lymphocyte population are increased, as are nonopsonized phagocytosis and lymphocyte-activated killer (LAK) cell activity. In the bronchoalveolar lavage fluid (BALF), a decrease occurs in total leukocyte counts, in particular the proportion and absolute number of lymphocytes, although the proportion of CD4⁺ T lymphocytes increases in comparison with CD8⁺ cells. The absolute number of macrophages in the BALF decreases, whereas the proportion and activation of macrophages increases. The LAK cell activity also increases in BALF.

An open, randomized clinical trial demonstrated that administration of two doses of *P. acnes* before shipping reduced more than 60% of the incidence of transport-stress induced respiratory disease compared with placebo-treated group. In two blinded, randomized clinical studies of horses with naturally occurring respiratory disease (characterized by fever associated with respiratory difficulty, and/or nasal discharge, cough, lymphadenopathy) treated with conventional therapy, 79% to 96% of the horses that received *P. acnes* recovered within 14 days of treatment, compared with 47% and 35%, respectively, of the horses from the placebo group.

MYCOBACTERIUM CELL WALL EXTRACT

The bacillus *Mycobacterium bovis* strain attenuated by Calmette and Guérin has been used all over the world as a vaccine against tuberculosis. In addition, *Mycobac-*

terium extracts are one of the most potent stimulants of macrophage function, resulting in subsequent release of cytokines (IL-1, TNF, colony-stimulating factors) and in lymphocyte activation. To this date, limited *in vitro* data exists that describes the effects of this immunomodulator in horse cells.

The immunotherapeutic agent Equimmune IV (Vetrepharm Research Inc., Athens, Ga.) is an USDA licensed oil-in-water emulsion of purified *Mycobacterium* spp. cell wall extract for the treatment of equine respiratory disease complex (ERDC) resulting from virus and/or bacteria. The recommended dose is 1.5 ml per animal intravenously. It has been approved for use in pregnant mares. Side effects after the immunotherapy include reaction at the injection site, fever, lethargy, and decreased appetite, likely related to the induced endogenous cytokine release. Four horses with a history of coughing were reported to develop severe inflammatory reaction in the respiratory tract (increased bronchial sounds, crackles, and wheezes in the lung fields, increased cell counts in BAL) after the immunomodulator administration, characterized by interstitial pneumonia, multifocal pulmonary granulomas and bronchiolitis, and subsequent development of lung fibrosis. In humans, although intravesical attenuated *Bacillus Calmette-Guérin* (BCG) immunotherapy has been used successfully in the treatment of bladder carcinoma, about 1% of patients develop systemic BCG infection (pneumonitis, hepatitis, renal insufficiency) or hypersensitivity reactions (disseminated pulmonary and hepatic granulomas characterized by noncaseating epithelioid granuloma with Langhans-type giant cells and lymphocytes) a few weeks after immunotherapy.

A randomized, double-blind clinical study of *Mycobacterium* spp. cell wall extract was conducted in horses with naturally occurring respiratory disease (fever, cough, nasal discharge, increased respiratory sounds, ocular discharge, decreased appetite, or performance). Results suggested that 83% of the horses receiving one intravenous dose of purified extract recovered from respiratory clinical signs in a shorter period of time (7 days) than the placebo group. In addition, only 40% of the horses receiving placebo recovered by 10 days of treatment.

PARAPOXVIRUS OVIS

The use of poxvirus as an immunostimulant originated from observations after the smallpox eradication program, in which vaccinated human patients presented improvement of viral diseases and tumors. Since then, the mechanism of action of parapoxviruses in the immune system has been studied, and the viral envelope is thought to contain proteins that promote the activation of NK cells, enhance phagocytic activity, and increase the release of interferon- α and IL-2.

Baypamun HK (Bayer AG, Leverkusen, Germany) is the form of purified and chemically inactivated parapoxvirus ovis strain D 1701 that is commercially available in Europe for use in horses and other domestic species. It is indicated for the prophylaxis of stress-induced respiratory diseases caused by transportation, hospitalization, and weaning; for the metaphylaxis and therapy of infectious diseases; and for enhancement of the immunization re-

sponse. The generally recommended dose is 2 ml per animal intramuscularly two or three doses 48 hours apart, before the stress is induced, immediately after birth or with conventional treatment for respiratory disease. Limited swelling at the injection site may occur.

In the horse, a blinded field study suggested that prophylactic administration of *Parapoxvirus ovis* to foals 6 and 4 days before weaning, plus at 5 days thereafter, assisted in preventing and reducing the incidence of respiratory disease from 24% to 7.9%. In a controlled field trial, Thoroughbred foals from the same farm received three doses of the immunotherapeutic drug or placebo immediately after birth, and 24 or 48 hours thereafter. These foals were monitored for 4 weeks, and 20% to 30% of the foals from the placebo group developed respiratory infections, whereas the foals in the groups receiving the immunomodulator did not. In addition, parapoxvirus ovis was suggested to minimize but not to prevent respiratory clinical signs (based on nasal exudate scores) in horses naturally challenged by contact with virulent equine herpes virus-1 or -4 (EHV-1 or EHV-4). A significantly greater proportion of young horses under stress induced by weaning, transportation, and commingling was more resistant to EHV-1 and EHV-4 infection, in addition to development of respiratory clinical signs when receiving parapoxvirus ovis, compared with the ones receiving placebo. To this date, limited *in vitro* data exist that describe the effects of this immunomodulator in horse cells.

CAPRINE SERUM FRACTION

Caprine Serum Fraction Immunomodulator (CSFI; Centaur, Inc., Overland Park, Kan.) is a USDA conditionally licensed immunomodulator for adjunct treatment of lower respiratory tract disease in horses. It is a sterile, filtered, purified, and standardized fraction of goat serum preserved in phenol and thimerosal. The label recommendation is 2 ml intramuscular injections, two applications, 7 to 10 days apart. Potential side effects are swelling and heat at the site of injection for 48 to 72 hours. A clinical efficacy trial in horses with unspecified lower respiratory tract disease (characterized by tracheal exudation) suggested improvement in the airway inflammation evaluated by an endoscopic examination score after two doses of the immunomodulator.

Phenotypical analysis of leukocyte subpopulations, phagocytosis and oxidative burst activity, LAK cell activity, and IL-2 receptor expression were evaluated in peripheral blood and BALF leukocytes after administration of two intramuscular injections of placebo or caprine serum fraction to six healthy yearling fillies. The results suggested immunomodulatory activity by the reduction of monocyte and CD8⁺ T lymphocyte counts in peripheral blood. In addition, the cellularity of bronchoalveolar lavage fluid was reduced after administration of the immunomodulator, particularly B lymphocyte counts and macrophages. Immune function tests including LAK cell activity, phagocytosis and oxidative burst activity, and IL-2 receptor expression did not detect changes after the administration of caprine serum fraction. Local and systemic reactions to the series of intramuscular injections of the product were characterized by mild swelling reaction at the intramuscular

injection site in one filly for 48 hours, and limb edema 24 hours after administration of the product in another filly. Elevation in body temperature in response to the immunotherapy was not detected by the scheduled daily physical examination.

A recent study examined the clinical application of this immunomodulator in horses diagnosed with "suppurative lower respiratory disease" based on endoscopic finding of bronchial discharge and at least one clinical evidence of respiratory disease (nasal discharge, abnormal lung sounds, cough, decreased performance). All horses were treated with antibiotics concomitantly and occasionally with dimethyl sulfoxide (DMSO). Two randomized dose response studies suggested that two intramuscular injections 1 week apart (day 0 and day 7) resulted in significant clinical improvement (clinical score based on exudate production, dyspnea, lung sounds, cough) by day 14 in the 60 mg or 120 mg CSFI-treated group compared with the placebo and lower dose-treated horses. No difference exists between 60 mg and 120 mg CSFI-treated groups. In a field study, 75% of horses treated with various antibiotics and two doses of CSFI recovered from their respiratory disease by day 21 compared with 35% of the animals receiving antibiotics and placebo. Hence some evidence exists that clinical recovery from lower respiratory tract infection may benefit from this immunomodulator. Further studies are warranted to characterize the efficacy of this product *in vivo*.

INTERFERON-ALPHA

The presence of viral products induces mononuclear phagocytes to produce endogenous interferon- α (IFN- α) in the early stages of infection. This type I interferon binds to a common receptor expressed on most of the cells and triggers intracellular signaling pathways that result in potent antiviral, immunomodulatory, and antiproliferative activities. Its antiviral effect is characterized by inhibition of viral protein synthesis, viral RNA degradation, activation of cytolytic activity of NK and LAK cells, increase in major histocompatibility (MHC) class I expression of virus-infected cells, enhanced IFN- γ expression by lymphocytes, macrophage activation, and dendritic cell maturation. Interestingly, once the antiviral and antiproliferative activities are triggered by IFN- α , they can be transferred cell-to-cell by direct contact in the absence of the product. Oral IFN- α acts directly on oropharyngeal-associated lymphoid tissues by activation of the antiviral state of lymphocytes. The altered lymphocytes act as amplifiers of this mechanism by transferring this enhanced biologic effects to naive lymphocytes homed in distant tissues, such as the respiratory tract.

Oral administration of low doses of IFN- α has therapeutic benefit for acute and chronic viral infections in human patients and animals. In a double-blind, randomized block design study of horses with inflammatory airway disease (characterized by poor performance and exudate in the upper and lower airway) in active training, 50 U of natural, human IFN- α given orally for 5 consecutive days reduced airway inflammation, pharyngeal lymphoid hyperplasia, nasal discharge, and cough compared with horses receiving placebo. Horses that received oral IFN- α

recovered their BALF to a noninflammatory cytologic profile, and the proportion of lymphocyte subpopulations caused by the immunomodulator was unchanged.

The use of commercially available recombinant human IFN- α -2a (Roferon-A, Roche Laboratories Inc., Nutley, N.J.), which contains only one subtype of IFN- α in contrast to the natural form, failed to reduce virus shedding and respiratory disease (fever, nasal and ocular discharge) in experimental herpes-virus-1 infection in horses. Whether the less protective effect of the immunotherapy regime used was due to inappropriate dosage or to differences in the response to the recombinant form is unknown. High doses of IFN- α are more likely to cause side effects because of induced self-destructive inflammatory responses and immunosuppression.

OTHER IMMUNOMODULATORS

Some immunomodulatory agents have been used for years in clinical patients, although their mechanism of action and effectiveness have not been established. Levamisole phosphate is a synthetic antihelmintic, which immunomodulatory properties have been characterized poorly *in vitro* and *in vivo*. However, cell mediated response and phagocytic activity may improve in immunocompromised individuals after immunotherapy. Extralabel use of levamisole (Levasole, Ripercol L), 2 mg/kg, orally, every 48 hours in horses as an adjunct for treatment of respiratory disease is based on clinical reports of prevention and treatment of chronic respiratory infections in children and neonate animals. Other immunostimulants largely used in human medicine for the prophylaxis and treatment of respiratory disease include combined lyophilized fractions of several common respiratory tract bacterial pathogens and bacterial ribosomal fractions. In addition, the expansion in the use of pure cytokines such as IL-2, IL-12, IL-18, TGF- β , TNF and IFN- γ as immunomodulatory agents became possible because of advances in recombinant DNA technology.

As the field of veterinary immunology evolves and more clinical trials are available, the understanding of the complex interactions among the immune mediators in developing a balanced immune response allows a more effective use of immunomodulators in the prevention and treatment of respiratory diseases without adverse effects, either to enhance protection against pathogens or to decrease airway hyperreactivity.

Supplemental Readings

- Biron CA: Interferons α and β as immune regulators—a new look. *Immunity* 2001; 14:661-664.
- Cormack S, Alkemade S, Rogan D: Clinical study evaluating a purified mycobacterial cell wall extract for the treatment of respiratory disease. *Equine Pract* 1991; 13:18.
- Evans DR, Rollins JB, Huff GK et al: Inactivated *Propionibacterium acnes* (Immunoregulin) as adjunct to conventional therapy in the treatment of equine respiratory diseases. *Equine Pract* 1988; 10:17.
- Flaminio M, Rush B, Shuman W: Immunologic function in horses after nonspecific immunostimulant administration. *Vet Immunol Immunopathol* 1998; 63:303-315.

- Lindner A, von Wittke P, Thein P et al: Effect of paramunity inducer on the incidence of diseases and the plasma cortisol content in Thoroughbred foals before and after weaning. *Tierarztl Prax* 1993; 21:47-50.
- Moore BR: Clinical application of interferons in large animal medicine. *J Am Vet Med Assoc* 1996; 208:1711-1715.
- Moore BR, Krakowka S, Cummins JM et al: Changes in the airway inflammatory cell populations in Standardbred racehorses after interferon-alpha administration. *Vet Immunol* 1996, 49:347-358.
- Nestved A: Evaluation of an immunostimulant in preventing shipping related respiratory disease. *J Equine Vet Sci* 1996; 16:78.
- Rush BR, Flaminio MJBF: Immunomodulation in horses. *Vet Clin North Am Equine Pract* 2000; 16:183-197.
- Vail CD, Nestved AJ, Rollins JB et al: Adjunct treatment of equine respiratory disease complex (ERDC) with *Propionibacterium acnes*, immunostimulant, EqStim. *J Equine Vet Sci* 1990; 10:399.
- Ziebell KL, Steinmann H, Kretzdorn D et al: The use of Baypamun N in crowding associated infectious respiratory disease: efficacy of Baypamun N (freeze dried product) in 4-10 month old horses. *J Vet Med [B]* 1997; 44:529-536.

SECTION IX

Eye Diseases

Edited by Dr. David T. Ramsey

CHAPTER 9.1

Examination of the Eye

IAN P. HERRING
Blacksburg, Virginia

Examination of the eye should be included as a part of every physical and prepurchase examination. The completeness of the examination will be guided by the experience of practitioner and the availability of specialized instrumentation. Although information presented in this chapter is intended to provide the practitioner with knowledge required to examine the eye competently, some of the techniques described herein may be limited to individuals with specialized training and/or instrumentation. An appreciation of normal ocular anatomy is required to correctly diagnose ocular abnormalities. Therefore general notations regarding normal equine ocular anatomy and normal anatomic variation are also provided. Because there is substantial variation in appearance of the normal equine eye, years of experience may be necessary before an examiner is comfortable differentiating variations of normal from an abnormality. Comparison with the fellow eye in the same horse is often useful in making such distinctions.

OPHTHALMIC INSTRUMENTATION AND EXAMINATION TECHNIQUES

Focal Light Source

Use of a penlight is rarely sufficient for examination; use of a bright light source, such as a Finoff transilluminator, is generally recommended. Use of some form of magnification, such as a head loupe, in conjunction with a bright light source is also useful. Effective eye examination requires variation in the angles and distances between the light source, examiner's vantage point, and horse's eye. When held parallel with the examiner's line of sight and the tapetal or fundic reflection through retroillumination is used, opacities of the transparent ocular tissues or fluids (tear film, cornea, aqueous fluid, lens, vitreous humor) that obstruct light become apparent. Directing the light at an angle 90° to the examiner's line of sight will high-

light subtle opacities of the cornea—such as ulcers, scars, striae, and lipid or mineral deposits.

Slit Lamp Biomicroscope

A portable slit lamp biomicroscope provides the examiner a magnified image of external ocular structures (including adnexa, conjunctiva, cornea, and sclera), anterior chamber, iris, iridocorneal angle, lens, and anterior vitreous. Examination of the central and posterior vitreous and the ocular fundus cannot be performed by use of the slit lamp biomicroscope without use of special lenses. The slit lamp examination provides the examiner a level of detail that cannot be acquired by use of any other equipment. Detecting subtle abnormalities such as aqueous flare and cell, determining the depth at which corneal or lens opacities occur, and accurately estimating the thickness of the cornea or depth of corneal ulceration are benefits of use of the slit lamp.

Direct Ophthalmoscopy

When used to examine the ocular fundus, the direct ophthalmoscope provides a virtual, upright image that is magnified approximately eight times in the horse. The pupil should be dilated before ophthalmoscopy is performed. With direct ophthalmoscopy only a small portion of the fundus is viewed at a time; thus the examiner must systematically vary the field of view to examine the entire fundus, and then create a mental montage of the ocular fundus. To visualize the fundus, the circular dial of condensing lenses should be adjusted to 0 diopters and, from a distance of 0.5 to 1 m, the tapetal reflex visualized. The examiner should then move to within 2 to 3 cm of the cornea to bring the retinal image into focus. The dioptric setting of the ophthalmoscope may have to be adjusted slightly (between -2 to +2) to obtain clear focus. Distant direct ophthalmoscopy is a technique used to detect opac-

ities of the cornea, lens, and vitreous that obstruct light produced by the ophthalmoscope. After dilating the pupil, the examiner stands at an arm's distance from the horse's eye, adjusts the circular dial of condensing lenses to 0 diopters, places the instrument against his/her brow, and observes the reflection through the ophthalmoscope. Opacities of the transparent ocular tissues or fluids appear as dark spots in the tapetal reflection.

Indirect Ophthalmoscopy

Indirect ophthalmoscopy provides a large field of view in comparison to direct ophthalmoscopy and allows more rapid examination of the entire fundus. A light source and handheld condensing lens are required. The light may be a handheld source (Finoff transilluminator) or a specialized headset that incorporates a light source. A headset also incorporates a prism that splits the images returning to the right and left eye of the examiner, thereby providing stereopsis. Held at an arm's distance from the horse's eye with the light source held adjacent to the examiner's eye, the light beam is directed into the eye of the horse, and a tapetal reflection is observed. The converging lens is then introduced into the path of light at a distance of approximately 2 to 5 cm from the corneal surface. The lens should be shifted closer or further from the corneal surface until a clear image fills the lens. The lens should be held perpendicular to the beam of light and then tilted slightly until light reflections from the anterior and posterior surface of the condensing lens are nearly lined up over each other. Tilting the lens excessively may cause aberration of the image. Indirect ophthalmoscopy provides a real, inverted image of the fundus that appears rotated 180 degrees (upside down).

Topical Dyes

Fluorescein Sodium

Fluorescein sodium dye has several applications in ophthalmic diagnostics. Most commonly, it is applied topically to detect corneal ulceration, wherein the dye will adhere to exposed corneal stroma but not to intact corneal epithelium. The dye appears as an apple-green fluorescent color when stimulated by a cobalt blue light source (available on many direct ophthalmoscopes). Nasolacrimal patency and leakage of corneal wounds may also be evaluated with topical fluorescein sodium dye.

Rose Bengal

Rose bengal dye is used less often than fluorescein sodium dye but may be used to detect devitalized epithelium and to diagnose tear film disorders, including keratoconjunctivitis sicca and tear film mucin deficiency. Dye uptake may also occur with equine herpesvirus keratitis and early fungal keratitis.

RESTRAINT OF THE HORSE FOR OPHTHALMIC EXAMINATION

In uncooperative horses, a combination of intravenous sedation, motor nerve blocks, and topical anesthetic will facilitate examination. A nose twitch is occasionally re-

quired. For sedation, a short-acting drug such as xylazine (0.5-1.0 mg/kg IV) or detomidine (0.005-0.2 mg/kg IV) is generally adequate. For ophthalmic diagnostic purposes, nerve blocks that achieve eyelid akinesia are most useful. Several methods are described, but this author prefers to inject 1 to 2 ml of 2% lidocaine with a 25-gauge needle over the palpebral nerve as it crosses the dorsal aspect of the zygomatic arch. The palpebral nerve may be palpated in this region by gently strumming the tip of the index finger vertically over the zygomatic arch. Akinesia occurs within 1 to 5 minutes, depending on injection volume and precision of injection. Duration is variable but may last up to 2 to 3 hours. Application of topical ophthalmic anesthetics (e.g., 0.5% proparacaine) may be required for diagnostic procedures—including tonometry, nasolacrimal lavage, and corneconjunctival scrapings for cytologic examination.

EXAMINATION OF THE EYE

When possible, ophthalmic examination should be performed in a quiet environment capable of being darkened. Examination in a brightly lit environment may obscure abnormalities of the clear ocular media or tissues. The order or sequence in which the ophthalmic examination and diagnostic tests are performed is often critical because performing one diagnostic test may obscure results of subsequent tests. Examples are listed below.

Neuroophthalmic Examination

Palpebral and Corneal Reflexes

The palpebral and corneal reflexes evaluate the functional integrity of cranial nerves V and VII. The palpebral reflex is evaluated by lightly touching the periocular region. The examiner should note the speed and completeness of eyelid closure. The corneal reflex is performed by lightly touching the corneal surface with a cotton swab. A normal response involves retraction of the globe and closure of the eyelids.

Oculocephalic Reflex

The oculocephalic reflex evaluates the vestibular pathways, medial longitudinal fasciculus, and cranial nerves that innervate the extraocular muscles, including cranial nerves III, IV, and VI. While the horse's head moves from side to side and then up and down, the resultant ocular movements should be noted. The normal response is physiologic nystagmus with the fast phase in the direction of head movement.

Pupillary Light Reflex

The pupillary light reflex (PLR) tests the afferent function of the retina, optic nerve, and optic tracts, as well as the efferent function of cranial nerve III (parasympathetic component) and iris sphincter muscle function. The PLR should be evaluated in the dark and prior to sedation or instillation of topical mydriatic drugs. Before evaluating the PLR, the examiner should evaluate pupil symmetry. If the examiner stands 2 m directly in front of the horse and uses a direct ophthalmoscope (set at 0 diopters), simultaneous viewing of the tapetal reflection from both eyes is

possible. This should be performed in ambient light and in the dark. Differences in pupil size (anisocoria) should be noted. To evaluate the PLR, a bright focal light source is directed into one eye, and the degree of constriction of the ipsilateral pupil (direct PLR) is noted. The examiner then quickly shifts the light source to illuminate the contralateral eye and observes the degree of constriction already present (consensual PLR) as well as the increased constriction that should occur upon direct stimulation. The magnitude of the consensual PLR is minimal in the horse. Use of a dim light source will diminish the speed and completeness of the PLR, as will fear or excitement in a horse. A normal PLR does not confirm vision because vision is a cortical phenomenon, not a reflex.

Evaluation of Vision

The ability of a horse to navigate a series of obstacles in its pathway or in an unfamiliar environment may help characterize functional vision deficits. When practical, this should be performed in a variety of lighting conditions. The menace response provides a crude estimate of vision in an individual eye. Bringing a hand deliberately into the horse's field of view or gesturing towards its eye while keeping the contralateral eye covered evaluates the menace response. It is important not to stimulate a tactile response by causing excessive air movement or by touching the vibrissae. The menace response may not be fully developed until a horse is 2 to 3 weeks of age. The dazzle reflex is the normal response to a bright light stimulus directed into the eye and involves retraction of the globe and closure of the eyelids. Because the dazzle reflex is a subcortical phenomenon, it is valuable in clinically distinguishing cortical causes of blindness from blindness related to diseases of the retina, optic nerve, or optic tracts.

EXAMINATION OF THE OCULAR ADNEXA

Examination for anatomic or physiologic abnormalities of the eyelid should be performed with illumination and magnification when necessary. A prominent sulcus located above and parallel with the eyelid margin divides the upper and lower eyelids into orbital and tarsal components. Numerous lashes are present on the lateral two-thirds of the upper eyelid. Normally, the lashes are directed nearly perpendicular to the corneal surface. A variable number of vibrissae are found along the base of the lower eyelid and at the medial aspect of the base of the upper eyelid. Close examination of the eyelid margins will reveal numerous small openings of the meibomian (tarsal) glands, approximating 40 to 50 in the upper and 30 to 40 in the lower eyelid. When the eyelids are everted slightly, the meibomian glands are visible through the palpebral conjunctiva as ivory to white opaque lines oriented perpendicularly to the eyelid margin.

During examination of the conjunctival surfaces, signs of hyperemia, chemosis, and/or follicle formation should be noted. The palpebral conjunctiva adheres tightly to the eyelid, whereas the bulbar conjunctiva is loosely adherent and freely movable over the surface of the sclera. The bulbar conjunctiva is normally transparent except where it is pigmented. The conjunctiva adjacent to the limbus is often pigmented, as is the temporal bulbar conjunctiva. The

lacrimal caruncle is a variably sized, smooth, raised conjunctival structure that resides at the medial aspect of the palpebral fissure. The caruncle is usually darkly pigmented and may have fine hairs emanating from its surface.

With the exception of its leading edge, the nictitating membrane is normally retracted in the inferonasal orbit. The leading edge is usually pigmented, although lack of pigmentation may be normal in horses with negligible periocular pigmentation. Retraction of the globe results in passive movement of the nictitating membrane across the surface of the cornea. Retropulsion of the globe into the orbit (by pressing on the eye through the upper eyelid) causes protrusion of the nictitating membrane, thus facilitating examination of its palpebral surface. The bulbar aspect of the nictitating membrane may be examined by carefully grasping the leading margin with forceps and everting it by applying gentle outward traction. Sedation, auriculopalpebral nerve block, and topical anesthetic are generally required.

EXAMINATION OF THE LACRIMAL SYSTEM

Assessment of aqueous tear production is accomplished by the Schirmer tear test (STT). Although the STT is rarely performed in the horse, indications include a dry, lackluster appearing cornea and chronic keratoconjunctivitis of unknown cause. The test is performed by placing a commercially available STT strip between the cornea and lower eyelid at a position near the junction of the lateral and middle third of the lower eyelid. Normal values in the horse are extremely variable but are generally quite high. As commercially available STT strips are often completely saturated within one minute, it has been recommended that 30-second measurements be made; normal values are reported at ≥ 20 mm/30 seconds. The STT should be performed before sedation or application of topical solutions, including anesthetics.

Evaluation of the lacrimal drainage apparatus includes visual inspection of the upper and lower lacrimal puncta (located 8-9 mm from the medial canthus on the conjunctival side of the eyelid margin) and the nasal punctum (located medially on the floor of the nasal vestibule near the mucocutaneous junction). Physiologic patency of the nasolacrimal duct is evaluated by instilling fluorescein sodium dye onto the ocular surface and observing passage of dye through the nasal punctum. Passage may take up to 5 minutes in the normal horse. Anatomic patency may be evaluated by use of a nasolacrimal cannula attached to a syringe filled with irrigating solution (saline solution). Topical anesthetic solution is instilled, and the cannula is inserted gently into the upper or lower puncta and respective canaliculus. The puncta that is not cannulated is then occluded by digital pressure, and the solution is irrigated into the nasolacrimal duct through the nasal punctum. Alternatively, this may be accomplished more easily by retrograde cannulation of the nasal punctum with a urinary catheter (5 Fr). The catheter is advanced 3 to 4 cm, and 20 to 40 ml saline solution is gently flushed by syringe while reflux through the nasal punctum is prevented with digital pressure. Irrigated fluid should be observed passing from the lacrimal puncta. Sedation is often required before nasolacrimal irrigation.

EXAMINATION OF THE CORNEA

The cornea is examined with a focal light source with or without supplementary magnification. Slit lamp examination provides additional subtle detail, including approximation of corneal thickness and depth of corneal lesions. The normal cornea of a mature horse is horizontally ovoid and measures 28 to 32 mm horizontally, 23 to 26 mm vertically, and approximately 0.7 to 0.8 mm thick. The nasal aspect of the cornea is vertically broader than the temporal aspect. The normal cornea should be optically clear, devoid of vasculature, and nonpigmented. A thin gray to white line is noted at the corneoscleral junction medially and laterally and represents trabecular attachments of pectinate ligament to the posterior cornea. Subtle corneal opacities may be overlooked unless a variety of illumination techniques are used during corneal examination. Initially diffuse focal illumination should be directed perpendicular to the cornea and nearly parallel with the observer's visual axis. While the observer maintains the same vantage point, the light source should then be directed obliquely—then nearly perpendicularly—to the corneal surface to highlight subtle or inconspicuous lesions. Topical fluorescein sodium dye will identify corneal ulceration.

EXAMINATION OF THE ANTERIOR CHAMBER

The anterior chamber is examined with a focal light source (with or without supplementary magnification) and a slit lamp biomicroscope. The depth of the anterior chamber (the distance between the posterior cornea and the lens-iris diaphragm) and the clarity of the aqueous humor should be determined. Abnormal depth of the anterior chamber may indicate a shift in the normal position or a change in volume of the crystalline lens. Normal aqueous humor is optically clear. Uniform turbidity of this fluid (aqueous flare) is an indication of an abnormally high protein or cellular content. Focal cloudiness may indicate the presence of vitreous humor or fibrin in the anterior chamber. Slit lamp examination permits detection of subtle aqueous flare, which may not be appreciated without use of this instrument.

A readily available and inexpensive alternative to a slit lamp biomicroscope that may be used to determine depth of the anterior chamber and clarity of the aqueous humor is a direct ophthalmoscope dialed to the smallest spot aperture. The instrument is held approximately 1 cm from the horse's central cornea. The examiner does not view through the instrument but instead gains a vantage point perpendicular to the direction of the light beam. This permits the examiner to observe the light beam as it traverses the cornea, aqueous humor, and anterior portion of the crystalline lens. Reflections should be observed at interfaces between the air-tear film (corneal reflection) and the aqueous humor-anterior lens capsule (lens reflection). Light should not be visible passing through the aqueous humor. If the examiner observes a homogeneous light beam passing through the aqueous humor (e.g., "light in the fog"), aqueous flare is present. The ventral aspect of the anterior chamber should be inspected for settled (gravitational) cellular debris.

EXAMINATION OF THE IRIS

The iris is most frequently a shade of brown in color but may also be gold, blue, or white. There may be color variation between the two irides or multiple colors within an iris (heterochromia iridis). When constricted, the pupillary aperture in the horse is horizontally oval in the adult but nearly round in the neonate and round in both neonates and adults when dilated. At the dorsal pupillary margin are the corpora nigra (granula iridica), a series of prominent, variably sized, heavily pigmented uveal bodies. Inferiorly, the corpora nigra are also present but are much less prominent. Occasionally, corpora nigra are absent in a normal eye. Close examination of the iris using oblique illumination reveals a textured surface with numerous small furrows and folds. Persistent pupillary membranes (remnants of embryonic vasculature) always emanate from the iris collarette of the iris surface and are commonly detected in normal eyes.

The peripheral iris may be visualized nasally and temporally where trabeculae of the iridocorneal angle extend from the iris surface to the cornea. Use of a gonioscope is not necessary to examine the nasal and temporal iridocorneal angle.

EXAMINATION OF THE LENS

Complete examination of the lens requires pharmacologic mydriasis. This author recommends topical use of 1% tropicamide solution. The lens should be examined for opacification, shifts in position, and size. The normal lens should be optically clear. In older horses, the entire lens is yellow in color, and nuclear sclerosis may be evident but should not obstruct the passage of light. Light-obstructing lens opacities should be recorded with regard to size, density, and location. Such opacities can be detected readily by distant direct ophthalmoscopy (described above). Examination of the lens with a slit lamp biomicroscope will allow detection of extremely small lens opacities and facilitate localization of opacities. The peripheral edge (equator) of the lens should not be visible. Visualization of the equator of the lens may indicate lens instability (subluxation, luxation), microphakia (congenitally small lens), or lens coloboma.

EXAMINATION OF THE POSTERIOR SEGMENT

Topical application of 1% tropicamide achieves mydriasis, which may last 4 to 8 hours in the normal horse. Multiple applications (2-3) of tropicamide, 3 to 5 minutes apart, will induce more rapid and complete dilation of the pupil. Longer-acting mydriatics, such as atropine sulfate, are slow-acting, have a longer duration of action, and should not be used for diagnostic purposes.

Examination of the vitreous humor is accomplished using a focal light source, slit lamp, or direct ophthalmoscope. Normal vitreous humor is an optically clear, gel-like body. Dense opacities within the vitreous or liquefaction of the vitreous are abnormal and should be noted. Hyaloid artery remnants may be detected in horses up to 4 months of age.

The equine fundus may be examined using a transilluminator alone, although substantially greater detail may

be observed using direct or indirect ophthalmoscopy. Topographically, the equine fundus is divided into a tapetal zone (tapetum lucidum), which is located in the dorsal half of the fundus, and a nontapetal zone. The tapetal zone is roughly triangular and may be yellow, green, or blue. Absence of the tapetum lucidum is a variation of normal. The nontapetal region is generally heavily pigmented, although complete or partial lack of pigmentation in the nontapetal zone is common in light colored horses and eyes with blue irides. Lack of pigmentation or scant pigmentation permits visualization of the choroidal vasculature. A stellate arrangement of large veins (vortex veins) is often visible in lightly colored fundi. The equine optic disc is invariably located in the nontapetal fundus. The optic disc is located slightly ventral and lateral to the posterior pole of the globe. The optic disc is horizontally ovoid in the adult and more round in young horses. The optic disc is salmon pink, and the inferior margin of the disc is often irregular. Approximately 40 to 60 small retinal blood vessels radiate from the periphery of the optic disc, and retinal arterioles, and venules cannot be differentiated clinically. The vascular pattern of the equine retina is clas-

sified as paurangiotic, with blood vessels extending only a short distance from the optic disc. Retinal vasculature that originates from the disc in the horizontal meridian extends approximately 2 disc diameters from the disc, whereas vasculature in the vertical meridian extends approximately 1 disc diameter from the disc. End-on tapetal emissaria and choriocapillaris vasculature appears as numerous, small uniformly distributed black dots ("Stars of Winslow"). A wide range in the clinical appearance of the normal fundus exists, and differentiating between variations of normal and abnormal is often difficult.

Supplemental Readings

Barnett KC, Crispin SM, Lavach JD et al: Examination of the eye and adnexa. In Barnett KC, Crispin SM, Lavach JD et al: Color Atlas and Text of Equine Ophthalmology, pp 9-21, London, Mosby-Wolfe, 1995.

Cooley PL: Normal equine ocular anatomy and eye examination. Vet Clin North Am Equine Pract 1992; 8:427-449.

Lavach JD: Large Animal Ophthalmology, St Louis, Mosby, 1990.

CHAPTER 9.2

Equine Vision and Optics

PAUL E. MILLER
Madison, Wisconsin

Equine veterinarians are often asked to determine how well a particular horse can see or to estimate whether a horse is suitable for high-performance, visually-oriented activities such as hunting/jumping and 3-day eventing. Although preserving vision is often the driving force in the treatment of many ocular diseases, the visual capabilities of normal horses, let alone those with ocular disease, are not well understood. This chapter describes the normal constituent parts of equine vision: the ability to perceive light, motion, and contrast; visual perspective and field of view; depth perception; visual acuity; and color vision, but the complete visual experience is a synthesis of all these components into a unified perception of the environment. In general, the visual capabilities of horses with ocular disease are commonly diminished from normal.

SENSITIVITY TO LIGHT

The equine visual system has evolved to function well under nocturnal conditions but also has several features that improve vision in bright light. For example, the nuclear region of the equine lens contains yellow pigments, as do

human lenses and those of other highly diurnal species such as squirrels. These pigments filter out shorter (blue) wavelengths of light, similar to yellow tinted sunglasses for humans, thereby reducing glare in bright light and improving the contrast of some objects against their background. The large *corpora nigra* on the central, superior border of the iris also improve vision in bright light by enhancing pupillary constriction and acting as an "internal visor" which blocks direct sunlight exposure of the inferior retina, thereby further reducing glare.

The horse's vision in dim light is improved by a large, superiorly located, triangular, reflective *tapetum lucidum* deep to the retina, which reflects light back through the retina and provides the photoreceptors a second opportunity to capture each quantum of light. The color of the tapetum is the result of regular spacing of collagen fibrils in the choroid and is not attributable to pigments in these fibers. Regions of the tapetum where collagen fibers are more numerous are more highly reflective and produce yellow or green reflections, whereas thinner regions tend toward deep blue to purple reflections. Although the tapetum improves vision in dim light, it also scatters light and reduces the eye's potential visual acuity. Nevertheless, the

be observed using direct or indirect ophthalmoscopy. Topographically, the equine fundus is divided into a tapetal zone (tapetum lucidum), which is located in the dorsal half of the fundus, and a nontapetal zone. The tapetal zone is roughly triangular and may be yellow, green, or blue. Absence of the tapetum lucidum is a variation of normal. The nontapetal region is generally heavily pigmented, although complete or partial lack of pigmentation in the nontapetal zone is common in light colored horses and eyes with blue irides. Lack of pigmentation or scant pigmentation permits visualization of the choroidal vasculature. A stellate arrangement of large veins (vortex veins) is often visible in lightly colored fundi. The equine optic disc is invariably located in the nontapetal fundus. The optic disc is located slightly ventral and lateral to the posterior pole of the globe. The optic disc is horizontally ovoid in the adult and more round in young horses. The optic disc is salmon pink, and the inferior margin of the disc is often irregular. Approximately 40 to 60 small retinal blood vessels radiate from the periphery of the optic disc, and retinal arterioles, and venules cannot be differentiated clinically. The vascular pattern of the equine retina is clas-

sified as paurangiotic, with blood vessels extending only a short distance from the optic disc. Retinal vasculature that originates from the disc in the horizontal meridian extends approximately 2 disc diameters from the disc, whereas vasculature in the vertical meridian extends approximately 1 disc diameter from the disc. End-on tapetal emissaria and choriocapillaris vasculature appears as numerous, small uniformly distributed black dots ("Stars of Winslow"). A wide range in the clinical appearance of the normal fundus exists, and differentiating between variations of normal and abnormal is often difficult.

Supplemental Readings

Barnett KC, Crispin SM, Lavach JD et al: Examination of the eye and adnexa. In Barnett KC, Crispin SM, Lavach JD et al: Color Atlas and Text of Equine Ophthalmology, pp 9-21, London, Mosby-Wolfe, 1995.

Cooley PL: Normal equine ocular anatomy and eye examination. Vet Clin North Am Equine Pract 1992; 8:427-449.

Lavach JD: Large Animal Ophthalmology, St Louis, Mosby, 1990.

CHAPTER 9.2

Equine Vision and Optics

PAUL E. MILLER
Madison, Wisconsin

Equine veterinarians are often asked to determine how well a particular horse can see or to estimate whether a horse is suitable for high-performance, visually-oriented activities such as hunting/jumping and 3-day eventing. Although preserving vision is often the driving force in the treatment of many ocular diseases, the visual capabilities of normal horses, let alone those with ocular disease, are not well understood. This chapter describes the normal constituent parts of equine vision: the ability to perceive light, motion, and contrast; visual perspective and field of view; depth perception; visual acuity; and color vision, but the complete visual experience is a synthesis of all these components into a unified perception of the environment. In general, the visual capabilities of horses with ocular disease are commonly diminished from normal.

SENSITIVITY TO LIGHT

The equine visual system has evolved to function well under nocturnal conditions but also has several features that improve vision in bright light. For example, the nuclear region of the equine lens contains yellow pigments, as do

human lenses and those of other highly diurnal species such as squirrels. These pigments filter out shorter (blue) wavelengths of light, similar to yellow tinted sunglasses for humans, thereby reducing glare in bright light and improving the contrast of some objects against their background. The large *corpora nigra* on the central, superior border of the iris also improve vision in bright light by enhancing pupillary constriction and acting as an "internal visor" which blocks direct sunlight exposure of the inferior retina, thereby further reducing glare.

The horse's vision in dim light is improved by a large, superiorly located, triangular, reflective *tapetum lucidum* deep to the retina, which reflects light back through the retina and provides the photoreceptors a second opportunity to capture each quantum of light. The color of the tapetum is the result of regular spacing of collagen fibrils in the choroid and is not attributable to pigments in these fibers. Regions of the tapetum where collagen fibers are more numerous are more highly reflective and produce yellow or green reflections, whereas thinner regions tend toward deep blue to purple reflections. Although the tapetum improves vision in dim light, it also scatters light and reduces the eye's potential visual acuity. Nevertheless, the

tapetum confers a distinct survival advantage to the horse as many of its natural predators also have a tapetum. The cellular tapetum of the cat reflects up to 130 times more light than the human fundus, and although the fibrous equine tapetum is not as efficient as the cat's, its abilities are still undoubtedly superior to that of humans. This suggests the threshold for light detection in horses is much less than that in humans but not as low as in many of its predators.

The horse has a number of other adaptations that improve vision in dim light. In addition to a very large cornea that permits large amounts of light into the eye, in dim light the horse's pupil dilates to an area 6 times larger than a human's (3-3.5 times greater than a cat's or dog's) to allow even more light to reach the retina. The elongated pupil, typical of the horse, is common in nocturnal species because in bright light this shape closes more completely in comparison with a round pupil, thereby providing additional protection for a highly light-sensitive retina. The equine retina also has 9 to 20 times as many rod photoreceptors, which function best in dim light, as it does cone photoreceptors, which function best in bright light. Finally, as in many species adapted for vision in dim light, equine rhodopsin continues to increase in sensitivity to light (dark adapt) for a relatively longer period of time than that of a human.

SENSITIVITY TO MOTION

Horses, like humans, are more sensitive to moving objects than they are to stationary objects. This is especially true for objects in the horse's peripheral visual field, which has a visual acuity so low that it permits detection of only "motion" and "brightness" rather than discrete objects. Poor visual acuity coupled with a "prey-mentality" may explain why horses often shy from seemingly innocuous objects in their peripheral visual field. It is also possible that the broadening of the equine retina in the horizontal meridian increases motion detection by a "barrel distortion" optical aberration. In this aberration, a circular image moving from the central to peripheral retina is distorted into a larger ellipse that also appears to move more quickly across the retina, thereby increasing its chances of detection. It is likely, however, that because horses lack a fovea, motion-detecting abilities of humans in bright light are superior to those of horses because photoreceptors located in the human fovea are more densely packed.

CONTRAST SENSITIVITY

In general, objects that have a low degree of contrast with their background are more difficult to see than highly contrasted objects are, even if the objects are the same size and viewed from the same distance. Bright light also may impair the visual discriminating abilities of the rod-rich equine retina. One study reported that a 2.54-cm wide stimulus was more visible to a horse on an overcast day than was a 5.08-cm stripe on a sunny day. Contrast stimuli underfoot also seemed to be less visible to younger horses than to older horses. Examination of head and neck carriage showed that younger horses did not lower their heads as much as older horses with more training.

VISUAL PERSPECTIVE AND FIELD OF VIEW

A horse that is grazing has a very different visual perspective than one that is standing with its head upright. Additionally, head height above the ground varies substantially between breeds. A field of tall grass appears as dense, impenetrable brush to a Miniature Horse, and as a wide-open savannah to a Clydesdale horse.

The lateral position of the eyes in the skull affords the horse a wide, panoramic view. Additionally, the nasal extension of the retina and comparatively greater vertical width of the pupil nasally than temporally further enhances the temporal peripheral visual field of the horse. Based on anatomic relationships, the horse is believed to have a total monocular visual field in the horizontal meridian (i.e., the portion of the horizon that can be seen by an eye when fixed on one point) of approximately 190 to 195 degrees and up to 178 degrees in the vertical (superior to inferior) meridian. When the visual fields of the two eyes are combined, the total horizontal visual field is up to 350 degrees, and the horse has virtually a complete sphere of vision around its body. The extent of binocular overlap is probably 55 to 65 degrees, although some suggest it may be as great as 70 degrees and up to 80 degrees anterior and below the nose.

Several minor "blind spots" exist in the visual field of the horse, as follows: the width of the horse's head directly behind it, superior and perpendicular to the forehead, directly below the nose, and a small oval region in the superior visual field where light strikes the optic nerve itself are "blind spots." Clearly it is very difficult for a predator, or human handler, to "sneak-up" on a horse despite the presence of these areas.

DEPTH PERCEPTION

Depth perception is enhanced when the visual fields of the two eyes overlap. Merely viewing an object with both eyes simultaneously, however, does not guarantee improved depth perception. Stereopsis (binocular depth perception) results when the two eyes view the environment from slightly different vantage points and the two images are fused into one. If the two images are not fused, double vision may occur and depth perception is very difficult to achieve. Animals and humans with only one eye, however, still have the ability to perceive depth, and many horses with only one eye still can effectively jump barriers. Monocular depth perception clues include relative brightness, size, contour, areas of light and shadows, object overlay (closer objects block distant ones), linear and aerial perspective (parallel lines converging onto a vanishing point), density of optical texture (texture decreases with distance), and motion parallax.

Horses seem to be able to use static monocular clues to recognize depth in the two-dimensional photographs and are even susceptible to some of the pictorial visual illusions humans are. Clearly, being able to use monocular clues to estimate depth is a distinct advantage to the horse because its monocular visual fields are so large. Nevertheless, two eyes are better than one as the binocular threshold for depth perception in horses is five times better than that for one eye. Humans still have better depth perception than horses, however. From two meters away humans

can detect a few-mm difference in depth, whereas horses are able to detect a difference of only 9 cm from the same distance. Horses may rotate their noses upward to observe distant objects because binocular overlap is oriented down the nose.

VISUAL ACUITY

Visual acuity refers to the ability to see the details of an object separately and without blurring. Interpretation of these images depends on the optical properties of the eye, the retina's ability to detect and process images, and the ability of higher visual pathways to interpret these images. In normal animals, visual acuity is usually limited by the architecture of the retina.

OPTICAL FACTORS THAT AFFECT VISUAL ACUITY

Refractive State

In humans, failure of the clear optical media (cornea, lens, and vitreous) to properly focus light on the retina commonly results in refractive errors and astigmatism (an unevenly focused image on the retina). Refractive errors require correction with contact lenses or spectacles if the visual potential of the eye is to be realized. A focus of light in front or behind the retina results in a myopic (near-sighted) or hyperopic (farsighted) refractive error, respectively. The extent of this error is expressed by the following formula:

$$\text{Diopter} = \frac{1}{f}$$

where f is the focal length (in meters) of the optical system. Therefore an eye that is 2 diopters (D) myopic at rest is in focus $\frac{1}{2}$ meter in front of the eye.

The average resting refraction of the horse is near emmetropia (normal), but some horses are significantly (≥ 3 D) myopic or hyperopic, and horses with aberrant visual behavior attributable to refractive errors have been described. In general, when the refractive error approaches 2D, most humans will report a noticeable improvement in their vision with corrective lenses. Astigmatism is uncommon in normal horses but can be severe in horses with corneal disease.

Loss of the focusing power of the lens, as occurs after lens extraction, results in severe hyperopia (10D) and a marked reduction in visual acuity. Setting a direct ophthalmoscope to -10 D and viewing the room through the view-port can simulate this degree of hyperopia. Surprisingly, although 10D hyperopia is debilitating to some horses, most are still able to visually orient in their environment and are capable of negotiating jumps, especially when guided by an experienced rider. They would not, however, be able to perform more visually challenging tasks without a corrective contact or intraocular lens.

Accommodation

Adjustable focusing (accommodation) is needed if objects at different distances are to be viewed with equal clarity.

In general, because of the optics of the equine eye, only a small change in the degree of refraction by the lens (<2 D, or <1 D in either direction) is needed to maintain a focused image on the retina.

Retinal Factors in Visual Acuity

Enhanced vision in dim light typically requires a greater number of photoreceptors to synaptically converge on a single ganglion cell. In humans the peak ratio is 1:1, whereas in horses the ratio is several times greater. Although this convergence improves vision in dim light, it also reduces visual acuity, just as high-speed film produces a "grainy" image in daylight.

The topographic distribution of the photoreceptors is also different between humans, who have a densely packed fovea temporal to the optic disc, and horses, which lack a fovea. Ganglion cells—and presumably the photoreceptors—of horses are most dense in a 1-mm wide horizontal band located approximately 3 mm superior to the disk in or near the tapetal zone and extending 22 mm in the nasal and temporal directions. In the temporal half of this visual streak, ganglion cell density increases slightly, but an indistinct field of relatively high density also continues along the nasal arm to near the ora ciliaris retinae. As in all species, substantially fewer ganglion cells exist at the periphery of the retina than in the center, thus significantly reducing the visual acuity of the peripheral visual field. It is believed that this long, narrow streak conforms to the projection of the horizon on the retina and provides a particularly acute image of this part of the environment. The temporal portion of the streak provides the greatest visual acuity, and perhaps some color vision as this region may have a slightly increased density of cones. The tapetal location of the streak further enhances vision in dim light—but at the expense of light scattering and degraded visual acuity in bright light. Although the horse has the lowest ganglion cell density of the domestic mammals, its very large eye means that its total number of ganglion cells—and hence information-carrying capacity—are comparable to that found in humans.

ESTIMATES OF VISUAL ACUITY

The Snellen fraction is a common method of describing visual acuity in humans; the normal person has a visual acuity of 20/20. This value means that the test subject can discern from 20 feet away the details of an image (letters on a chart) that a normal person also could differentiate from 20 feet away. When this scheme is applied to animals, the visual acuity of the dog is approximately 20/75, and the cat is 20/100 to 20/200. Peak equine visual acuity varies from about 20/30 on behavioral testing, 20/35 to 20/40 based on ganglion cell density calculations, and approximately 20/60 based on electrophysiologic testing. This means that from 20 feet away, a normal horse can distinguish details of an object that a person with normal vision could differentiate from 30 to 60 feet. In horses the most common methods of evaluating vision—such as the menace response or following cotton balls—are very crude because they test the motion sensitivity of virtually the entire retina. Positive responses with these techniques

may still be present even if visual acuity is less than 20/800 and a person is legally blind. It is also important to understand that the ability to distinguish details of an object is less important for a horse's lifestyle than for that of a human; improved vision in dim light allows the horse to exploit an ecologic niche inaccessible to humans.

Loss of the lens from cataract surgery (aphakia) may have less of an impact on visual acuity in the horse than in other species, particularly humans. Because the horse has a large eye, each receptor field may be up to 5 times larger than the receptor field of a human. Therefore the optical blurring attributable to aphakia in horses stimulates far fewer new receptor fields than in people and may be less detrimental to visual acuity.

COLOR VISION

Although very few studies of equine color vision exist, it is very likely that horses perceive colors differently from most, if not all, mammals, including humans. Color vision depends upon the presence of at least two types of color-sensitive cone photoreceptors. In normal humans three such cone types are present: red, green, and blue. The differential stimulation of these cells results in a broad spectrum of color perception. Most mammals, including

horses, are believed to have only two cone types (dichromatic color vision) and many fewer cones than humans have. Histologically, horses have a rich population of blue cones and electrophysiologically, horses also appear to have a cone that is intermediate to the human red and green cones. Behaviorally, horses can be trained to reliably differentiate blue and red versus gray without regard to reflectance (brightness) but have much more difficulty in discriminating green or yellow from gray; indeed, sometimes they are not able to discriminate them at all. In addition to being dichromatic, it is likely that color is less intense to horses as well (Color Plates 1 and 2).

Supplemental Readings

- Harman AM, Moore S, Hoskins R et al: Horse vision and an explanation for the visual behavior originally explained by the "ramp retina." *Equine Vet J* 1999; 31:384-390.
- Timney B, Macuda T: Vision and hearing in horses. *J Am Vet Med Assoc* 2001; 218:1567-1574.
- Roberts SM: Equine vision and optics. *Vet Clin North Am Equine Pract* 1992; 8:451-457.
- Ver Hoeve JN, Neitz J, Murphy CJ: Horse sense: electrophysiologic measures of equine vision. *Invest Ophthalmol Vis Sci* 1999; 40(Suppl):22.

CHAPTER 9.3

Ocular Therapy

MICHAEL J. BLAIR
Richmond, Virginia

Ocular therapy for the horse presents several unique and interesting challenges. The principles of therapy are the same as for other species; however, the method of drug delivery may necessitate ingenuity to provide effective treatment that is safe for the equine patient and for the personnel who are administering treatment. This chapter will focus on some of the basic principles of ocular therapy as well as on practical methods of drug delivery for ocular tissues.

The most basic concept of drug therapy is the delivery of an appropriate drug in an effective concentration to the target ocular tissue. The drug should be minimally harmful to nondiseased tissues that it contacts. The effectiveness of a drug with respect to its toxicity is often called the *therapeutic index*. A narrow therapeutic index indicates that the effective dose or concentration is close to the toxic level, thereby necessitating careful clinical and/or laboratory monitoring.

Pharmacologic treatment of ocular disease is divided arbitrarily into local and systemic modes of drug delivery. Local treatment is further subdivided into topical, subconjunctival, intraocular, and intralesional or perilesional

modes. When developing a plan for effective drug delivery, it is helpful to divide the eye into two anatomic compartments. The anterior segment consists of the cornea and anterior sclera, aqueous humor, iris, ciliary body, and crystalline lens. The posterior segment is composed of the vitreous body, retina, choroid, optic nerve, and posterior sclera. In general, topical and subconjunctival delivery is only effective for treatment of anterior segment abnormalities. The most practical delivery of drug to the posterior segment is systemic administration. Because many ocular diseases concurrently affect tissues of the anterior and posterior segment, a combination of systemic and local treatment commonly is necessary.

LOCAL THERAPY

Topical Treatment

Topical administration of drug is the most important and commonly used treatment modality for the majority of ocular diseases in horses. However, several important concepts

may still be present even if visual acuity is less than 20/800 and a person is legally blind. It is also important to understand that the ability to distinguish details of an object is less important for a horse's lifestyle than for that of a human; improved vision in dim light allows the horse to exploit an ecologic niche inaccessible to humans.

Loss of the lens from cataract surgery (aphakia) may have less of an impact on visual acuity in the horse than in other species, particularly humans. Because the horse has a large eye, each receptor field may be up to 5 times larger than the receptor field of a human. Therefore the optical blurring attributable to aphakia in horses stimulates far fewer new receptor fields than in people and may be less detrimental to visual acuity.

COLOR VISION

Although very few studies of equine color vision exist, it is very likely that horses perceive colors differently from most, if not all, mammals, including humans. Color vision depends upon the presence of at least two types of color-sensitive cone photoreceptors. In normal humans three such cone types are present: red, green, and blue. The differential stimulation of these cells results in a broad spectrum of color perception. Most mammals, including

horses, are believed to have only two cone types (dichromatic color vision) and many fewer cones than humans have. Histologically, horses have a rich population of blue cones and electrophysiologically, horses also appear to have a cone that is intermediate to the human red and green cones. Behaviorally, horses can be trained to reliably differentiate blue and red versus gray without regard to reflectance (brightness) but have much more difficulty in discriminating green or yellow from gray; indeed, sometimes they are not able to discriminate them at all. In addition to being dichromatic, it is likely that color is less intense to horses as well (Color Plates 1 and 2).

Supplemental Readings

- Harman AM, Moore S, Hoskins R et al: Horse vision and an explanation for the visual behavior originally explained by the "ramp retina." *Equine Vet J* 1999; 31:384-390.
- Timney B, Macuda T: Vision and hearing in horses. *J Am Vet Med Assoc* 2001; 218:1567-1574.
- Roberts SM: Equine vision and optics. *Vet Clin North Am Equine Pract* 1992; 8:451-457.
- Ver Hoeve JN, Neitz J, Murphy CJ: Horse sense: electrophysiologic measures of equine vision. *Invest Ophthalmol Vis Sci* 1999; 40(Suppl):22.

CHAPTER 9.3

Ocular Therapy

MICHAEL J. BLAIR
Richmond, Virginia

Ocular therapy for the horse presents several unique and interesting challenges. The principles of therapy are the same as for other species; however, the method of drug delivery may necessitate ingenuity to provide effective treatment that is safe for the equine patient and for the personnel who are administering treatment. This chapter will focus on some of the basic principles of ocular therapy as well as on practical methods of drug delivery for ocular tissues.

The most basic concept of drug therapy is the delivery of an appropriate drug in an effective concentration to the target ocular tissue. The drug should be minimally harmful to nondiseased tissues that it contacts. The effectiveness of a drug with respect to its toxicity is often called the *therapeutic index*. A narrow therapeutic index indicates that the effective dose or concentration is close to the toxic level, thereby necessitating careful clinical and/or laboratory monitoring.

Pharmacologic treatment of ocular disease is divided arbitrarily into local and systemic modes of drug delivery. Local treatment is further subdivided into topical, subconjunctival, intraocular, and intralesional or perilesional

modes. When developing a plan for effective drug delivery, it is helpful to divide the eye into two anatomic compartments. The anterior segment consists of the cornea and anterior sclera, aqueous humor, iris, ciliary body, and crystalline lens. The posterior segment is composed of the vitreous body, retina, choroid, optic nerve, and posterior sclera. In general, topical and subconjunctival delivery is only effective for treatment of anterior segment abnormalities. The most practical delivery of drug to the posterior segment is systemic administration. Because many ocular diseases concurrently affect tissues of the anterior and posterior segment, a combination of systemic and local treatment commonly is necessary.

LOCAL THERAPY

Topical Treatment

Topical administration of drug is the most important and commonly used treatment modality for the majority of ocular diseases in horses. However, several important concepts

must be considered. A drug administered topically must penetrate the ocular surface to establish a therapeutic concentration in the intended target ocular tissue. This factor is less important for a diseased surface ocular tissue—that is, the conjunctiva and superficial cornea. When deep corneal disease such as a stromal abscess or intraocular disease (e.g., iridocyclitis), is evident, selecting a drug that penetrates the surface is essential. The ability of a topically administered drug to penetrate the tissues depends on a number of factors—including drug concentration, partition coefficient (water/lipid solubility), contact time, and integrity of the corneal epithelium. The degree to which an agent penetrates the cornea may be influenced substantially by the hydrophobic corneal epithelium. Most drugs will penetrate the corneal stroma readily when the corneal epithelium is absent as a result of ulceration. When the corneal epithelium is intact, lipid-soluble drugs penetrate more readily than polar or water-soluble drugs. Ocular pharmaceutical manufacturers use this factor by producing drug products in a suspension that contains a lipid soluble molecule, which increases the penetrability of the drug. Drugs available in a solution of a salt product (e.g., sodium phosphate) generally do not penetrate as readily as suspensions (Box 9.3-1).

Increased (fortified) drug concentrations, prolongation of contact time by increasing the viscosity of the medication, and manual disruption of the integrity of the corneal epithelium can be used in specific clinical applications to improve penetrability of some drugs.

An important consideration in topical ocular treatment is the frequency of administration because this directly influences contact time and drug concentration in the target ocular tissues. Because of copious reflex tearing in horses, frequent administration (up to q2h) may be necessary to maintain therapeutic concentrations at the ocular surface. When uncertainty regarding the frequency of administration exists, frequent treatment is generally better, provided that the medication has a low tissue toxicity or side effect. The drug vehicle also influences the retention time of the medication at the administration site. Ophthalmic ointments generally have a longer retention time than solutions and suspensions; however, not all drugs are avail-

able in an ointment form. Ointments are generally easier to instill, have a longer retention time than solutions have, and are therefore the formulation of choice when the interval between treatments is prolonged. The viscosity and surface tension of the vehicle will influence the retention and contact time as well as the absorption of solutions and suspensions. Most commercially available ophthalmic drug preparations attempt to maximize these properties for optimal treatment. For these reasons an artificial tears product is preferable to dilute extemporaneously prepared medications to reduce surface tension and increase viscosity. Fortified concentrations of medications can also be helpful in maintaining therapeutic concentrations at the target site (Table 9.3-1).

Topical Drug Delivery Techniques

Topical administration in the horse may be difficult if the eye is painful or if the horse is uncooperative. When use of a topical solution or suspension is warranted and a delivery device is not available, a relatively simple technique of administration can be utilized. A topical ophthalmic solution may be drawn into a syringe fitted with a 25-Ga or 27-Ga needle. The needle is then broken off at its hub. The medication can then be squirted onto the surface of the eye. In many cases, use of a drug delivery device is the best method to ensure that an appropriate dosage and frequency of treatment are administered consistently.

Ocular Lavage Systems

Lavage tubing for intermittent or continuous perfusion of the ocular surface is the most commonly used type of

BOX 9.3-1

Topical Ocular Drugs and their Relative Corneal Penetrability

Superior Corneal Penetration

prednisolone acetate suspension
dexamethasone suspension
chloramphenicol
ciprofloxacin
ofloxacin

Inferior Corneal Penetration

prednisolone sodium phosphate
dexamethasone sodium phosphate
neomycin
tobramycin
gentamicin

Table 9.3-1
Formulation of Fortified Antibiotic Drugs for Topical Use

Drug	Preparation	Final Concentration
amikacin	Combine 250 mg amikacin with 15 ml artificial tears.	15 mg/ml (15%)
ampicillin	Reconstitute 1 gm with 5 ml sterile water. Combine with 15 ml artificial tears.	50 mg/ml (5%)
cefazolin or cephalothin	Reconstitute 1 gm with 5 ml sterile water. Combine with 15 ml artificial tears.	50 mg/ml (5%)
gentamicin	Combine 100 mg 15 ml artificial tears.	6 mg/ml (0.6%)
tobramycin	Combine 100 mg with 15 ml artificial tears.	6 mg/ml (0.6%)

device. Commercially available (Mila International, Erlanger, Ky.) or home-produced lavage tubing devices are relatively simple to place in the standing horse. Type I (single-entry) or type II (double-entry) lavage tubing devices are available. For type I devices, placement through the upper lateral or lower medial conjunctival fornix is recommended to prevent corneal trauma associated with poor tube placement or tubing dislodgment. A simple home-produced device can be made using a clear 5 or 8 French polyethylene feeding tube. A 10- or 12-Ga needle with the hub removed may be used as a trocar for transpalpebral tube placement. Rigid tubing, such as polypropylene, is not recommended because it may cause severe corneal ulceration if it becomes dislodged and contacts the cornea.

Deep sedation is usually necessary to install the lavage tubing. An auriculopalpebral (motor) nerve block and a frontal nerve block (sensory) or local infiltrative anesthesia is recommended. Using digital guidance, the trocar needle is placed parallel and adjacent to a gloved finger into the conjunctival fornix. The trocar is then passed full-thickness through the medial aspect of the superior or inferior eyelid. For type I lavage systems, the tubing is threaded through the trocar so the footplate is seated deep into the conjunctival fornix and the trocar is withdrawn antegrade. For type II lavage systems, the trocar is passed a second time full-thickness through the upper eyelid approximately 2 cm lateral to the first placement. The tubing is then threaded up through the trocar, and the trocar is then removed so that a loop of tubing lies deep in the recess of the conjunctival fornix. One end of the tubing is tied in a knot to prevent retraction, and several holes are made in the tubing with a 25-Ga needle approximately 1 and 2 cm proximal to the knot. The tubing should be flushed with saline solution to ensure patency and appropriate hole placement. Short pieces of tape are secured around the tubing near eyelid entry and exit points and then are attached to the skin at several points by use of sutures, glue, or skin staples. A blunt injection needle fitted with an injection cap is then inserted into the tubing. The injection cap is attached to the halter. A lavage system should be monitored frequently to ensure proper function and tube placement. Dislodgment may lead to abrasion and ulceration of the cornea.

An alternative technique for a lavage tube is via retrograde placement in the nasolacrimal duct. Retrograde nasolacrimal lavage tubes dislodge more often than subpalpebral lavage tubes but are less likely to induce iatrogenic corneal trauma. The technique involves threading a 3 to 8 French rubber or polyethylene tube in a retrograde direction from the nasal opening of the nasolacrimal duct. The tube may be passed through a surgical opening in the false nostril and then secured to the skin lateral to the nostril.

Continuous perfusion devices may eliminate the need for frequent manual drug administration and may reduce labor of treatment. A limiting factor for this method is that multiple drug therapy requires drug compatibility so that drugs mixed together and placed in the reservoir do not precipitate or alter individual drug effectiveness. Alternatively, electronic peristaltic pumps may be used to deliver medications through lavage systems; however, the expense and risk of damage to the equipment by the

horse make this a less practical method. Use of a commercially available latex reservoir (Mila International, Erlanger, Ky.) is recommended. Medication(s) are injected into the reservoir to pressurize the reservoir, thereby affecting drug delivery through the lavage tubing to the ocular surface. Volume and rate of drug delivery is regulated by lavage tubing size. The reservoir can be attached to the halter under the intermandibular space. Regular monitoring is recommended because excessive pressure applied by the horse to the reservoir may result in rupture of the reservoir.

Subconjunctival Injection

A useful method to provide localized treatment with a drug is by subconjunctival injection. The standing horse should be sedated for this procedure. An auriculopalpebral nerve block is also recommended. The best location for the injection is just under the dorsal or temporal bulbar conjunctiva. Injections into the palpebral conjunctiva, nictitating membrane, or eyelids should not be done. With a 25- or 27-gauge needle, drug solutions or suspensions of a volume up to 1 ml may be administered. The vehicle in which the drug is dissolved or suspended determines the duration of the therapeutic concentration for the desired effect. Injectable solutions of drugs are generally released rapidly to the ocular tissues, and the duration is short, usually 24 hours or less. Therefore solutions are excellent choices for providing rapid, high concentrations in the ocular tissues for initiation of treatment. Injectable suspensions and emulsions are long-acting preparations that slowly release the active drug over a period of time. Injectable suspensions are less potent; however, the duration of effect with longer acting preparations can be up to 1 to 2 weeks. Longer-acting preparations usually have oils in the vehicle to slow the rate of absorption. On occasion these oils can incite an inflammatory response and formation of a granuloma at the injection site. Drug preparations designed for parenteral injection are most appropriate to administer by subconjunctival injection. Solutions that are formulated for topical use should never be administered by subconjunctival injection. Antibiotics, corticosteroids, and atropine are medications that often are administered subconjunctivally. This author has found subconjunctival injection of 0.5 to 1 ml of atropine 15 mg/ml to be extremely useful in initiating treatment for inflammatory ocular disease.

Subconjunctival Microosmotic Pumps

A promising new technique for treating horses is the implantation of a microosmotic pump (Alzet Corporation, Palo Alto, Calif.) into the subconjunctival space. The pump is a rigid structure about the size and shape of an average human oral capsule. The center of the device contains a drug reservoir surrounded by a hypertonic concentration of salt. When the pump is placed in an aqueous environment, fluid moves through the outer rigid membrane in the direction of the osmotic gradient created by the hypertonic salt. This in turn compresses the central reservoir to deliver the drug through a portal at the end of the device. The pump can provide continuous drug

treatment over a 7-day period. The procedure to implant the pump can be easily accomplished in a standing horse with the aid of sedation and an auriculopalpebral nerve block. A small pair of blunt-tipped tenotomy scissors cuts a 5-mm incision into the superior-temporal bulbar conjunctiva, 2 to 3 mm from the limbus. The conjunctiva is then undermined with the scissors to create a pocket for insertion of the pump into the subconjunctival space. After the pump is inserted, the incision is temporarily held closed with a small hemostat or other lockable fixation forceps to prevent expulsion of the pump. The incision is closed permanently using 5-0 absorbable suture in a simple continuous pattern. The pump is easily removed by making a small incision into the conjunctiva at the end of the pump and applying digital pressure to expel it. The main disadvantage of this technique is the small capacity of the pumps. The reservoir of the smallest and most useful pump is 100 microliters. Larger-capacity pumps are available but are difficult to implant in the subconjunctival space. Because of volume capacity limitations, drugs must be extremely concentrated to be effective. Larger pumps can be implanted subcutaneously, and tubing can be tunneled from the pump to the conjunctival cul de sac; however, this procedure is less practical.

Intracameral Injection

Although not routinely recommended, intracameral injections of drug into the aqueous or vitreous chambers may be necessary in some infectious diseases. Drugs that are too toxic when administered systemically or those that penetrate ocular tissues poorly after topical or systemic administration can be used in this method. Topical ocular preparations of drug should *never* be administered by intracameral injection. Injection should not be attempted in the standing horse. General anesthesia with the aid of a muscle-relaxing agent such as guaifenesin or diazepam is recommended. For injections into the anterior chamber, a 27- or 30-gauge needle attached to a syringe is used.

The needle is placed 1 mm posterior and perpendicular to the limbus at a 45-degree angle to the limbus. Using a drillinglike motion with gentle pressure, the needle is advanced through the conjunctiva and sclera into the anterior chamber, parallel to the iris. A volume of fluid equal to the volume of drug to be injected is withdrawn (usually 0.1-0.25 ml); the syringes are exchanged; and the drug is injected. The fluid removed may be submitted for cytologic analysis and/or microbial culture and susceptibility testing when indicated. Injections into the vitreous are made 10 to 12 mm posterior to the limbus through the sclera with the needle directed posteriorly so that the lens is not traumatized. A volume of vitreous humor equal to the volume of drug to be injected is first withdrawn, and then the drug is injected. Sustained-release implants have also been implanted in the vitreous cavity of the eye to provide prolonged therapy (see Chapter 9.5: "Equine Recurrent Uveitis").

Intralesional Therapy

Diseases of the adnexal tissues may be treated locally by direct injection into the target tissue (e.g., the eyelid). Eye-

Table 9.3-2

Relative Potency of Common Systemic Nonsteroidal Antiinflammatory Drugs with Respect to the Eye

Drug	Dose	Relative Potency
aspirin	30 mg/kg PO q8-24h	Low to medium
flunixin	0.5-1.1 mg/kg PO, IV, or IM q12-24h	High
melglumine ketoprofen	1.1-2.2 mg/kg IV q24h	Medium
phenylbutazone	2.0-4.4 mg/kg PO or IV q12-24h	Medium

PO, By mouth; q8-24h, every 8 to 24 hours; IV, intravenous; IM, intramuscular.

lid neoplasms may be treated with specific chemotherapeutic drugs (see Chapter 9.7: "Fungal Keratitis"). Some chemotherapy protocols use oil emulsions to promote immune stimulation and retention of the drug in the target tissue. Inflammatory diseases of the eyelids can also be treated with intralesional injections of long-acting corticosteroid preparations.

SYSTEMIC THERAPY

Systemic treatment for ocular diseases is a very important and occasionally disregarded treatment modality for inflammatory and infectious diseases. Pain is an important factor of ocular inflammation that should be considered. If left untreated, a horse in pain may cause further injury to the eye from self-induced trauma associated with rubbing. Antiinflammatory/analgesic medications play an important role in the treatment of the majority of eye diseases in the horse (Table 9.3-2). Nonsteroidal antiinflammatory drugs are more potent analgesics than are corticosteroid antiinflammatory drugs. Because risk of laminitis has been associated with systemic corticosteroid use, these agents are generally reserved for more severe inflammation and for horses that are refractory to non-steroidal antiinflammatory drugs. When corticosteroids are indicated, a single injection of dexamethasone may be used to initiate treatment. Oral corticosteroids can also be used. The uptake of prednisolone is more reliable than that of prednisone. These drugs are preferred over oral use of dexamethasone.

Antibiotics administered systemically are always indicated when rupture or perforation of the globe has occurred or when traumatic laceration of the eyelids and adnexal tissues is evident. They may also be indicated as prophylaxis before surgery and for corneal and intraocular infections, usually in combination with topical therapy. When using systemic antibiotics to treat ocular and periocular adnexal tissues, a basic tenant of pharmacology must be remembered: deliver an effective drug dose to the target tissue. A number of factors, including the vascular supply of the tissue, influence this principle with respect to the eye. Vascularity of the eyelids and periocular tissues is extensive; therefore a therapeutic blood level that is greater than the minimum inhibitory concen-

tration for an infectious organism should be effective in preventing or treating infections.

Permeability of the blood aqueous barrier is an important consideration when attempting to establish a therapeutic level of drug in intraocular tissues. Tight junctions of vascular endothelial cells within the eye may impede vascular permeability by drug molecules. Drug efficacy is substantially influenced by the ability of a drug to cross the blood aqueous barrier. Presence of uveal inflammation significantly increases ocular tissue permeability by drugs that normally would not penetrate ocular tissue barriers to establish a therapeutic level within the eye. The degree of altered permeability from inflammation is not predictable. Therefore the clinician should select a drug that has the greatest penetrability when an infectious organism is susceptible to more than one drug.

The cornea is normally avascular; therefore topically administered drugs reach intraocular tissues primarily through the aqueous humor and the precorneal tear film. For this reason topical treatment is usually essential for infectious corneal disease. Systemic antibiotic drugs are most useful in corneal infections after neovascularization of the cornea or surgical vascularization by use of a conjunctival pedicle graft. Deep corneal abscesses attributable to bacterial or fungal organisms may respond to systemic antimicrobial drugs if the drug achieves therapeutic levels in the aqueous humor and cornea. Many of the frequently used systemic antibiotics may not achieve therapeutic levels in intraocular tissues or fluids unless ocular inflammation is substantial (Box 9.3-2).

BOX 9.3-2

Frequently Used Systemic Antibiotics and their Abilities to Achieve Therapeutic Levels in Normal Ocular Tissues after Systemic Administration

Good Penetration

cefazolin
ampicillin
ciprofloxacin
enrofloxacin
trimethoprim-sulfamethoxazole
fluconazole

Poor Penetration

gentamicin
tobramycin
amikacin
erythromycin
itraconazole
ketoconazole

Supplementary Readings

- Brooks DE: Equine ophthalmology. In Gelatt KN: Veterinary Ophthalmology, 3rd edition, Baltimore, Lippincott Williams & Wilkins, 1999.
- Moroi SE, Lichter PR: Ocular pharmacology. In Hardman JG, Gilman A, Limbird LE (eds): Goodman & Gilman's the Pharmacological Basis of Therapeutics, 9th edition, New York, McGraw-Hill, 1996.
- Bartlett JD, Fiscella RG, Ghormley NR et al (eds): Ophthalmic Drug Facts, St Louis, Facts and Comparisons, 1998.

CHAPTER 9.4

Emergency Treatment of Ocular Trauma

MARY LASSALINE
Gainesville, Florida

An *ocular emergency* is defined as any condition that threatens or has caused loss of vision, ocular pain, loss or limitation of eyelid or ocular motility, or deformity of the globe, periorbital tissues, or orbit. Ocular emergencies constitute a small but important percentage of all emergencies. Domesticated horses are

prone to ocular injury by virtue of their temperament, prominent eyes, and the environment in which they exist. Ocular trauma in horses is observed infrequently but is most often attributable to kick injury by another horse; contact with a sharp branch, nail, metal feed rack, or whip; collision into a fence post, trailer, or stall wall;

tration for an infectious organism should be effective in preventing or treating infections.

Permeability of the blood aqueous barrier is an important consideration when attempting to establish a therapeutic level of drug in intraocular tissues. Tight junctions of vascular endothelial cells within the eye may impede vascular permeability by drug molecules. Drug efficacy is substantially influenced by the ability of a drug to cross the blood aqueous barrier. Presence of uveal inflammation significantly increases ocular tissue permeability by drugs that normally would not penetrate ocular tissue barriers to establish a therapeutic level within the eye. The degree of altered permeability from inflammation is not predictable. Therefore the clinician should select a drug that has the greatest penetrability when an infectious organism is susceptible to more than one drug.

The cornea is normally avascular; therefore topically administered drugs reach intraocular tissues primarily through the aqueous humor and the precorneal tear film. For this reason topical treatment is usually essential for infectious corneal disease. Systemic antibiotic drugs are most useful in corneal infections after neovascularization of the cornea or surgical vascularization by use of a conjunctival pedicle graft. Deep corneal abscesses attributable to bacterial or fungal organisms may respond to systemic antimicrobial drugs if the drug achieves therapeutic levels in the aqueous humor and cornea. Many of the frequently used systemic antibiotics may not achieve therapeutic levels in intraocular tissues or fluids unless ocular inflammation is substantial (Box 9.3-2).

BOX 9.3-2

Frequently Used Systemic Antibiotics and their Abilities to Achieve Therapeutic Levels in Normal Ocular Tissues after Systemic Administration

Good Penetration

cefazolin
ampicillin
ciprofloxacin
enrofloxacin
trimethoprim-sulfamethoxazole
fluconazole

Poor Penetration

gentamicin
tobramycin
amikacin
erythromycin
itraconazole
ketoconazole

Supplementary Readings

- Brooks DE: Equine ophthalmology. In Gelatt KN: Veterinary Ophthalmology, 3rd edition, Baltimore, Lippincott Williams & Wilkins, 1999.
- Moroi SE, Lichter PR: Ocular pharmacology. In Hardman JG, Gilman A, Limbird LE (eds): Goodman & Gilman's the Pharmacological Basis of Therapeutics, 9th edition, New York, McGraw-Hill, 1996.
- Bartlett JD, Fiscella RG, Ghormley NR et al (eds): Ophthalmic Drug Facts, St Louis, Facts and Comparisons, 1998.

CHAPTER 9.4

Emergency Treatment of Ocular Trauma

MARY LASSALINE
Gainesville, Florida

An *ocular emergency* is defined as any condition that threatens or has caused loss of vision, ocular pain, loss or limitation of eyelid or ocular motility, or deformity of the globe, periorbital tissues, or orbit. Ocular emergencies constitute a small but important percentage of all emergencies. Domesticated horses are

prone to ocular injury by virtue of their temperament, prominent eyes, and the environment in which they exist. Ocular trauma in horses is observed infrequently but is most often attributable to kick injury by another horse; contact with a sharp branch, nail, metal feed rack, or whip; collision into a fence post, trailer, or stall wall;

or accumulation of debris in the conjunctival fornix during a race.

When a sudden change in vision or the appearance of the eye is evident or when signs of acute ocular pain are observed, the veterinarian should attempt to determine whether ocular trauma has occurred. If trauma is diagnosed inappropriately or is treated in an untimely manner, permanent compromise to vision may occur; time is the critical factor. The goals of urgent treatment are to preserve vision, relieve pain, maintain function, and maximize cosmesis. A thorough ophthalmic examination (determined by the condition and temperament of the horse) should direct a rapid but accurate diagnosis and a plan of action that may include referral to a veterinary ophthalmologist. Because a plethora of ocular abnormalities may result from trauma, this chapter describes the emergency ocular examination, reviews manifestations of ocular trauma, and provides a list of drugs recommended for use in treatment of traumatic ocular emergencies (Table 9.4-1).

It is essential to expediently acquire a thorough history in the event of a potential ophthalmic emergency. The signalment, history, and presenting complaint as well as previous or current topical or systemic drugs being administered are important to consider in devising a diagnostic and treatment plan. Historical information should include the nature and duration of the trauma, treatment (if any), and the horse's tetanus vaccination status. A brief but imperative general physical examination is essential for all ophthalmic emergencies, specifically those that result from probable trauma.

EMERGENCY OCULAR EXAMINATION

Direct visual assessment of the head, orbit, and globe are recommended as the first step in the physical examination of a horse that has sustained ocular trauma. A hands-off direct visual inspection should determine whether asymmetry of the face, eyelids, or orbits is evident by comparing right and left sides. This procedure is done from a distance of one meter from the horse and from a vantage point directly in front of the horse. Use of a focal light source is imperative. The "normal" eye should then be examined first. Eyelid function and carriage should be evaluated. When ocular trauma is suspected but an obvious ocular abnormality is not readily evident, the most straightforward approach to the emergency examination is to begin with the periocular adnexa and orbit and then to progress from anterior to posterior segments to the ocular fundus in a systematic manner. The horse's visual status, pupillary size, shape, pupillary light reflexes, and dazzle responses should be evaluated. An attempt should be made to determine the site and extent of the injury. A thorough ophthalmic examination is always indicated, even when minor surface injury of the periocular tissues, eyelids, or conjunctiva attributable to ocular trauma is detected. Adjacent ocular or periocular tissues frequently sustain vision- or globe-threatening collateral injury despite relatively insignificant surface ocular injury.

Direct ophthalmic examination may be facilitated by adequate restraint and sedation. The obvious goal is to perform a thorough examination without endangering the eye, handler, or examiner. Inadequate sedation can

lead to disastrous vision-threatening consequences. The temperament and condition of the horse dictate the degree of restraint and sedation necessary. Forcing a struggling horse's eyelids open when it has a deep corneal laceration or ulcer may cause rupture of the cornea and expulsion of intraocular contents. Topical anesthetic (0.5% proparacaine HCl) and eyelid akinesia and anesthesia may be used to facilitate examination (see Chapter 9.1: "Examination of the Eye"). General anesthesia may be necessary for a complete examination if extensive orbital or ocular injuries are suspected.

The most common equine ophthalmic emergency is eye pain of unknown explanation, which may also present a substantial diagnostic challenge for the veterinarian. Clinical signs that typify ocular pain include excessive lacrimation, blepharospasm, ptosis (drooping of the eyelid), enophthalmos, and miosis. Chemosis and conjunctival hyperemia often accompany a painful eye and are usually secondary to an underlying ocular abnormality. Hyperemia of the conjunctiva and episclera is often disproportionate to the severity of the ocular abnormality in the horse; severity of hyperemia should never be used as a means to estimate severity of an ocular abnormality.

In descending order of probability, ocular pain is most frequently attributable to iridocyclitis, ulcerative and nonulcerative keratitis, conjunctival and corneal foreign objects, glaucoma, eyelid and/or conjunctival lacerations, and inflammatory orbital disease. A thorough ophthalmic examination may differentiate clinical diagnoses that have similar clinical signs. For example, both iridocyclitis and glaucoma typically present as a slightly hyperemic eye with pain and corneal edema, but these clinical diagnoses differ in the presentation of the pupil and in intraocular pressure. The pupil is usually miotic, and intraocular pressure is decreased with iridocyclitis. With acute glaucoma, the pupil is often dilated, and intraocular pressure is increased.

Fluorescein sodium dye should be instilled topically to evaluate the corneal epithelial integrity. When available, a slit lamp biomicroscope is recommended to examine the cornea, anterior chamber, crystalline lens, and anterior vitreous humor. When appropriate, the intraocular pressure (IOP) should be estimated by use of a TonoPen XL (Mentor O&O, Norwell, Mass.). The posterior segment should be examined by use of direct and indirect ophthalmoscopy.

ORBIT AND GLOBE

Horses have a complete bony anterior orbital rim. The dorsolateral and ventral aspects of the orbit caudal to the anterior rim consist of fascia supported by fat and muscle; elsewhere the orbit is entirely bone. Orbital trauma may result in concurrent blepharodema, lid and intraorbital hemorrhage, damage to periorbital soft tissues, iridocyclitis, periorbital fractures, globe proptosis, and globe rupture.

Periorbital fractures are diagnosed by physical examination by digital palpation, radiography, and computed tomography. Physical examination is often more useful diagnostically; facial asymmetry, epiphora, crepitus, pain on palpation, and epistaxis suggest the presence of a periorbital fracture even if radiographic abnormalities are not

Table 9.4-1
Commonly Used Drugs for Ocular Emergencies

Drug	Dosage	Description
Analgesics		
butorphanol	0.005 mg/kg IV	Opioid; also provides sedation; added to α_2 -adrenergic agonist as needed
detomidine	0.01 mg/kg IV	Also provides sedation; potent, long-lasting α_2 -agonist
flunixin meglumine	1 mg/kg IV q12-24h	NSAID
phenylbutazone	2 mg/kg PO q12-24h	NSAID
xylazine	0.3 mg/kg IV	Also provides sedation; short-acting α_2 -adrenergic agonist
Anesthetics		
lidocaine	0.5-5 ml of 2% SQ	Local anesthesia and akinesia
proparacaine	0.5% topically	Topical anesthesia; may induce minor superficial corneal irregularities; may decrease tear production
Antibiotics		
amikacin	15 mg/kg IV q24h	Bactericidal aminoglycoside; good against gram-negative bacilli, organisms resistant to gentamicin or tobramycin
bacitracin-neomycin-polymyxin B	oo topically q2-8h	Broad-spectrum bactericidal
chloramphenicol	1% oo topically q2-8h	Gram-positive spectrum
ciprofloxacin	0.3% os topically q2-8h	Broad-spectrum bactericidal fluoroquinolone; reserved for treatment of severe infections by sensitive organisms
doxycycline	10 mg/kg PO q12h	Bacteriostatic broad-spectrum; effective against <i>Leptospira</i> spp.
gentamicin	6.6 mg/kg IV q24h 0.3% os topically q2-8h	Bactericidal aminoglycoside; gram-negative spectrum, also gram-positive aerobes; nephrotoxic, ototoxic
potassium penicillin G	22,000 IU/kg IV q6h	Bactericidal; gram-positive spectrum
procaine penicillin G	22,000 IU/kg IM q12h	Bactericidal; gram-positive spectrum
tobramycin	0.3% os topically q2-8h	Gram-negative spectrum; use restricted to severe corneal infections, particularly <i>P. aeruginosa</i>
trimethoprim-sulfamethoxazole	5 mg/kg PO q12	Bacteriostatic, broad-spectrum
Anticollagenolytics		
acetylcysteine	10% os topically q1-4h	Contains α -macroglobulins; inhibits matrix metalloproteases, serine proteases; new, sterile, autogenous sample should be collected every 5 days and kept sterile and refrigerated
EDTA	0.05% os topically q2-4h	
Serum	Topically q2-q6h	
doxycycline	0.3% topically q2-6h	Must be compounded
Antifungals		
amphotericin B	1.5% os topically	Broad-spectrum polyene; poor intraocular penetration when given parenterally; poor corneal penetration topically
fluconazole	0.2% oo topically q4-8h 1mg/kg PO q12h	Imidazole
itraconazole	1% oo topically q4-8h 3 mg/kg PO q12h	Imidazole; high corneal concentration; compounded in ointment with 30% DMSO
miconazole	1% os topically q4-8h	Imidazole; excellent corneal penetration; also active against gram-positive cocci
natamycin	5% suspension topically q4-8h	Polyene; good initial antifungal therapy choice; effective against <i>Aspergillus</i> , <i>Fusarium</i> sp.
povidone-iodine	2% solution topically	Also antibacterial, antiviral, antiprotozoal
silver sulfadiazine	1% topical cream	Also antibacterial

IV, Intravenous; q12-24h, every 12 to 24 hours; PO, by mouth; NSAID, nonsteroidal antiinflammatory drug; SQ, subcutaneous; oo, ophthalmic ointment; os, ophthalmic solution; EDTA, ethylenediaminetetraacetic acid; DMSO, dimethyl sulfoxide; pm, as needed.

Continued

Table 9.4-1

Commonly Used Drugs for Ocular Emergencies—cont'd

Drug	Dosage	Description
Antiinflammatories		
dexamethasone	0.05-0.2 mg/kg IV q24h 0.1% oo topically	Corticosteroid; should not use if ulceration present
DMSO	1g/kg IV q12-24h 30% oo topically	Topical ointment compounded with itraconazole
flunixin meglumine	1 mg/kg IV q12-24h	NSAID; also provides analgesia
flurbiprofen	0.03% os topically	NSAID; also provides analgesia
phenylbutazone	2 mg/kg PO q12-24h	NSAID; also provides analgesia
Mydriatic/Cycloplegics		
atropine	1% oo topically	Parasympatholytic mydriatic cycloplegic; should be used q12h to q8h until pupil dilates then prn; should monitor for signs of colic
Tranquilizers		
butorphanol	0.005 mg/kg IV	Opioid; also provides analgesia; added to α -agonist as needed
detomidine	0.01 mg/kg IV	Also provides analgesia; potent long-lasting α_2 -agonist
xylazine	0.3 mg/kg IV	Also provides analgesia; short-acting α_2 -agonist

detected. Oblique projections silhouetting the area of greatest swelling are the most useful, and a contralateral oblique radiograph should be made for comparison. Topically and systemically administered antiinflammatory drugs—including flunixin meglumine, dexamethasone, and dimethyl sulfoxide (DMSO)—reduce pain and lid swelling. Topical corticosteroid drugs should be used only if the corneal epithelium is intact and eyelid function is normal. If the paranasal or maxillary sinuses are involved—as evidenced by a fluid line on radiography—the fracture is considered “open” and systemically administered antibiotic treatment is warranted. Closed fractures are also typically treated with systemically administered antibiotics. Surgical correction is required if bone fragments are depressed and threaten the globe or if severe periorbital damage is evident. Surgery may involve interosseous wiring, bone plating, and cancellous bone grafting. It is imperative to initiate surgical repair quickly because fibrous fracture callus begins within one week in horses and may substantially compromise fragment reduction.

Sharp or blunt trauma may cause rupture of the globe. Even if the globe is not perforated, blunt trauma to the globe may rapidly recess the iridocorneal angle and increase intraocular pressure or result in a scleral rupture beneath intact bulbar conjunctiva. Rupture of the globe occurs most commonly at the limbus where the sclera is thinnest. Corneal and scleral perforations require prompt medical treatment and surgical repair to prevent infectious endophthalmitis, hypotony, and phthisis bulbi. Immediate medical treatment of orbital trauma should include topical and systemic administration of analgesic drugs, nonsteroidal antiinflammatory and antibiotic

drugs, and topical mydriatic/cycloplegic drugs. Corticosteroid drugs are contraindicated.

Blunt head trauma may also result in globe proptosis, but this trauma is uncommon in the horse because of the complete bony orbital rim and deep orbit. Temporary tarsorrhaphy and antibiotic treatment (administered topically and systemically) are indicated for a proptosed globe, along with systemic analgesic and antiinflammatory drugs. The prognosis for return to vision after proptosis is poor in globes with an absent consensual pupillary light reflex, miosis with severe hypotony, or hyphema. If the optic nerve is obviously severed or the globe is severely damaged, enucleation is recommended.

EYELIDS AND CONJUNCTIVA

Eyelid lacerations are extremely common in horses. A complete ophthalmic examination is important when eyelid lacerations are detected because collateral ocular tissue damage—including orbital cellulitis or abscess, periorbital fractures, globe perforation, corneal damage, and uveitis—is common. In cases of eyelid lacerations, bacterial culture, susceptibility testing, and fungal cultures should be submitted. The wound should be cleaned and repaired promptly to prevent infection, lid deformity, and exposure-induced corneal damage. Small lacerations may be repaired under standing sedation and infiltrative anesthesia if the horse is cooperative. Anesthesia of the middle two-thirds of the upper eyelid may be accomplished by infiltration of local anesthetic around the supraorbital nerve. Approximately 2 ml of 2% lidocaine is filled in a syringe with a 25-gauge $\frac{1}{8}$ -inch needle and infiltrated into the

supraorbital foramen, which forms a small, palpable depression in the supraorbital process of the frontal bone, medial to its most narrow aspect. A line block along the lateral third of the dorsal orbital rim anesthetizes the lacrimal nerve. Anesthesia of the lower lid may be induced by infiltrating lidocaine around the infratrochlear nerve near the medial aspect of the ventral orbital rim and the zygomatic nerve at the lateral aspect of the ventral orbital rim. General anesthesia is recommended for repair of more extensive lacerations, specifically those with tissue loss.

Lacerations should be cleansed with dilute (2%) povidone-iodine solution; such detergent scrubs and rubbing alcohols are irritating to the conjunctiva and cornea. Their use is contraindicated. Only minimal debridement is generally necessary in eyelid lacerations because of extensive vascular supply to the eyelids. Tissue tags or pedicles should not be excised because tissue loss can result in exposure keratitis. Even avulsed eyelids that are completely desiccated will undergo canalization by new blood vessels after surgical repair. Surgical repair should involve a two-layer closure (a deep layer through the tarsus-palpebral conjunctiva and a superficial layer through the skin-orbicularis oculi muscle) to minimize scar tissue formation and achieve an optimal cosmetic and functional result. Perfect apposition of the lid margin is imperative. Medial canthal lacerations may damage the nasolacrimal canaliculi and interfere with tear drainage. The integrity of nasolacrimal drainage may be evaluated by fluorescein sodium dye passage from the puncta at the medial canthus to the distal nasal punctum of the nasolacrimal duct. If the nasolacrimal system is damaged, surgical repair is warranted. Lacerations of the upper eyelid are more significant than lower lid lacerations because of greater movement of the upper lid over the cornea; failure to achieve perfect eyelid margin and palpebral conjunctival apposition may result in corneal ulceration. Lacerations of the nictitating membrane should also be carefully and properly repaired to prevent corneal damage. The nictitating membrane should only be excised if it is severely damaged.

Postoperative medical treatment consists of topical and systemic administration of antibiotics, systemic analgesic/antiinflammatory drugs, topical mydriatic/cycloplegic drugs, and administration of tetanus toxoid. The cornea should be protected if the eyelids are swollen or deformed such that the cornea is exposed.

Foreign objects are a common cause of eyelid, conjunctival, and corneal damage and are often embedded under the eyelids, in the conjunctival fornix, cornea, or posterior to the nictitating membrane. The entire orbital rim, including the space posterior to the nictitating membrane, should be examined for foreign objects when an immediate cause of epiphora, blepharospasm, conjunctival hyperemia, or chemosis is not evident. Radiography may benefit localization of metal foreign bodies.

Blunt trauma, lacerations, foreign objects, and chemical burns to the conjunctiva may result in chemosis and hemorrhage. Conjunctival hemorrhage may indicate a scleral laceration. Failure to detect and properly treat a scleral tear obscured by overlying hemorrhagic conjunctiva may result in hypotony, phthisis bulbi, and blindness. Conjunctival chemosis and hemorrhage often accompany

keratitis and corneal trauma; therefore fluorescein sodium dye should be instilled topically when conjunctival hyperemia or chemosis is present. If these conditions persist, reevaluation for an underlying cause such as corneal ulceration, iridocyclitis, or glaucoma is done.

CORNEA

Corneal trauma may result in abrasion, ulceration, superficial or deep laceration, or full thickness perforation with iris prolapse. Varying degrees of iridocyclitis accompany nearly all forms of keratitis in the horse. Any corneal defect should be considered potentially vision-threatening because resident microbial flora of the ocular surface includes both bacterial or fungal organisms that may become opportunistic and result in bacterial or fungal keratitis. Appropriate medical and surgical treatment of corneal trauma should be instituted promptly. When ocular injury is suspected, the cornea should be evaluated by use of fluorescein sodium dye. Topical corticosteroids are contraindicated if the corneal epithelium is absent.

The type and extent of corneal damage dictate treatment. Samples for cytologic evaluation and microbial culture should be collected from all corneal injuries before treatment is instituted. Abrasions and superficial nonpenetrating lacerations should be treated with topically applied antibiotic and mydriatic/cycloplegic drugs and with systemically administered nonsteroidal antiinflammatory drugs. Severe corneal inflammation may result in stromal liquefaction or "melting" (Color Plate 3). Collagenases produced or activated by microbes (particularly *Pseudomonas* sp.), leukocytes and corneal epithelial cells may rapidly destroy corneal stroma. Autogenous serum may be applied topically to reduce collagenase activity in the cornea. Acetylcysteine, ethylenediaminetetraacetic acid (EDTA), and doxycycline also have anticollagenase activity and may be used topically to prevent corneal melting.

Deep corneal lacerations and full thickness perforations require combined medical and surgical treatment. Medical treatment includes topically applied antibiotics, mydriatic/cycloplegics, and anticollagenolytic drugs. Systemically administered antibiotics and nonsteroidal antiinflammatory drugs are also indicated. Topical ocular treatment may be achieved with minimal risk to the horse and handler by use of a subpalpebral lavage drug delivery system (see Chapter 9.3: "Ocular Therapy"). Topical solutions should be used instead of ointments when a full thickness laceration, perforation, or impending perforation is probable because petrolatum-based ointments may result in intractable granulomatous iridocyclitis if the ointment enters the anterior chamber. Deep lacerations require direct corneal suturing and may also require additional support of a conjunctival flap.

The prognosis for vision with full thickness corneal lacerations is related to wound length. Lacerations 15 mm or less that are restricted to the cornea are associated with more favorable visual outcomes, whereas lacerations greater than 15 mm that extend to, along, or beyond the limbus have a guarded to poor prognosis for vision. Perforations caused by sharp objects have a more favorable prognosis than those caused by blunt objects because they tend to produce more isolated wounds. Corneal perfora-

tions are always accompanied by iridocyclitis and are often associated with a shallow anterior chamber, hyphema, and iris prolapse.

Corneal stromal abscess and keratomycosis are both vision- and globe-threatening complications of corneal ulceration in the horse and should be considered ocular emergencies. Corneal abscesses develop after infectious (bacterial, fungal) microbes or reactive foreign material is inoculated onto or into the corneal stroma. Subsequently, the surface epithelial cells migrate over the defect trapping organisms or material in the stroma. Stromal abscesses typically appear as yellowish-white or ivory-colored stromal infiltrates with concurrent severe corneal edema and iridocyclitis. The lesion usually does not retain fluorescein sodium dye or only retains fluorescein in an area smaller than the entire lesion. Intensive medical treatment that consists of topically applied mydriatic/cycloplegic and antibacterial and antifungal antibiotics as well as systemically administered antibiotics and nonsteroidal antiinflammatory drugs is appropriate initially to treat superficial stromal abscesses, but if significant improvement does not occur within 2 to 3 days, surgical treatment may be indicated. Deep stromal abscesses are often fungal in origin and are best treated surgically by posterior lamellar or penetrating keratoplasty, in conjunction with aggressive medical treatment. Stromal abscesses may rapidly progress to severe, painful endophthalmitis and blindness and may require enucleation.

Fungal infection may also be associated with ulcerative keratitis, perforation, and iris prolapse. Ulcerative keratomycosis often begins with fungal infiltration of a corneal defect by either a resident commensal organism or an organism residing on a foreign body (e.g., plant origin). Typical initial clinical signs include photophobia, miosis, blepharospasm, and epiphora. Diagnosis is made by detecting fungal hyphae cytologically or histologically (Color Plate 4) or in culture from tissue specimens. Medical treatment of ulcerative keratomycosis should include topically applied topical antifungal drugs, antibiotics for concurrent bacterial infection, and topical mydriatic/cycloplegic drugs and systemically administered nonsteroidal antiinflammatory drugs to treat concurrent iridocyclitis. Iridocyclitis may be exacerbated after initiation of topical antifungal treatment due to sudden fungal death; thus treatment frequency may need to be adjusted empirically. Surgical treatment with either a conjunctival flap or penetrating keratoplasty is indicated for deep ulcers or those that do not respond to initial medical treatment.

In addition to mechanical trauma, the cornea may also be damaged by chemical or thermal injury. Many substances commonly used around horses—including insecticides, antiseptics, and grooming soaps—may cause ulcers upon contact with the cornea. Acid substances tend to cause less damage than alkali because epithelial and stromal proteins precipitate in acidic solutions; thus acids have poor corneal penetration compared with alkali substances. Alkalis may rapidly penetrate and result in descemetocoele or perforation as stromal collagen is denatured. Secondary glaucoma and iridocyclitis are common sequelae of alkali burns of the cornea. Chemical burns should be lavaged with saline or water immediately and continuously for 15 to 20 minutes. It is important to lavage the conjunctival fornices as

well as the cornea itself to completely remove the chemical. Topical treatment with mydriatic/cycloplegics, antibiotics, and anticollagenolytics, as well as systemic administration with analgesics/antiinflammatory drugs, are indicated. Severe burns may warrant a conjunctival or amniotic membrane graft. Tear insufficiency is a complication of chemical burns; therefore tear production should be monitored for clinical signs of dry eye. Thermal burns of the cornea are less common but may also result in associated iridocyclitis and collagenolysis. Thermal burns should be treated topically with mydriatic/cycloplegics and antibiotics and systemically with analgesic/antiinflammatory drugs. Conjunctival grafting may be indicated to protect the cornea if the eyelids are burned such that they do not function normally.

UVEA

Ocular trauma may damage the iris and ciliary body that results in hyphema and iridocyclitis. Common large-scale clinical signs of iridocyclitis (anterior uveitis) include miosis, aqueous flare and cell, ptosis, blepharospasm, excessive lacrimation, and posterior synechia. Intraocular pressure is typically low. Treatment should include topical mydriatic/cycloplegic drugs, topical corticosteroid and nonsteroidal antiinflammatory drugs, and systemic antiinflammatory drugs. If hyphema is present after ocular trauma, exercise should be restricted to minimize continued bleeding. If fibrin remains in the anterior chamber as hyphema resolves, tissue plasminogen activator (50-100 µg) can be injected intracamerally to induce lysis of the fibrin clot. Complications of unresolved hyphema include posterior or peripheral anterior synechia, secondary glaucoma, and phthisis bulbi.

Iris prolapse is associated with full-thickness corneal laceration, perforated corneal ulcers, and ruptured stromal abscesses (Color Plate 5). Iris prolapse should be referred to a veterinary ophthalmologist for surgical repair as soon as possible. Postoperative medical treatment should include topical administration of mydriatics/cycloplegic drugs, topical and systemic administration of antibiotics, and nonsteroidal antiinflammatory drugs. Persistent iridocyclitis and endophthalmitis are severe complications of iris prolapse. The prognosis for vision is reduced for perforating corneal lacerations greater than 15 mm in length that extend beyond the cornea; for corneal wounds accompanied by hyphema, bacterial or fungal infection, or keratomalacia—and chronic corneal perforations of longer than two weeks' duration.

GLAUCOMA

Glaucoma in horses is diagnosed infrequently and invariably occurs secondarily to iridocyclitis. Clinical signs of glaucoma in horses may be inconspicuous. Ultimately, glaucoma is a blinding disorder; therefore early diagnosis and treatment are imperative (see Chapter 9.9: "Equine Glaucomas").

LENS

Ocular emergencies that involve the crystalline lens are uncommon in horses. Opacification (cataract) or instabil-

ity (subluxation, luxation) of the lens are common sequela to inflammatory ocular conditions. Rapidly forming cataracts may result in acute vision loss. The most common cause of cataracts and lens instability in horses is chronic iridocyclitis and/or concurrent inflammatory zonulysis. However, severe blunt or penetrating ocular trauma may result in lens subluxation or luxation, rupture of the lens capsule, and secondary cataract. Removal of a luxated lens may be warranted if the position of the lens causes pupillary block glaucoma or corneal edema. The latter is caused by the lens contacting the corneal endothelium. The prognosis is guarded for surgical removal of a luxated lens because secondary glaucoma and intractable iridocyclitis often occur postoperatively. Rupture of the lens capsule results in phacoclastic iridocyclitis and is considered a surgical emergency. The prognosis is guarded for surgical removal of cataracts that have formed secondary to iridocyclitis.

RETINA AND OPTIC NERVE

Retinal detachment is an uncommon complication of severe head trauma, cataracts, iridocyclitis, or perforating wounds to the globe. The area of detached retina loses function and subsequently degenerates rapidly. Focal retinal detachments do not usually result in clinically detectable vision impairment. A complete (total) exudative retinal detachment results in blindness and appears fundoscopically as a free-floating opaque veil over the optic disc. The ultrasonographic appearance of a complete retinal detachment is characteristic. The retina billows anteriorly into the vitreous cavity and away from the choroid and sclera but remains attached at the posterior pole around the optic disc and peripherally anterior to the equator by the ora ciliaris retinae, thereby producing a V or "seagull" shape. The detached retina may exhibit slow and sinuous aftermovements. Extensive retinal detachments can cause iridocyclitis and cataracts as well as blindness. Surgical correction of retinal detachments has not been reported in the horse.

Blunt head trauma may damage the optic nerve and result in acute blindness. A concussive force to the poll (e.g., from rearing and hitting a beam or rearing over backward and striking the back of the head on the ground) creates caudal movement of the brain inside the skull. Because

the optic nerves are fixed at the optic canals, the *contra coup* force causes the intracranial portion of the optic nerve (caudal to the optic canal) to stretch and rupture optic nerve axons. The immediate clinical result of this optic nerve damage is a dilated, fixed pupil, absence of a menace response, and an acutely blind eye. Initially, the fundus appears normal, or mild peripapillary retinal hemorrhage may be evident. The eventual result is attenuation or absence of retinal vasculature and a pale optic disc. The goal of immediate posttraumatic medical treatment is to reduce pain and swelling by use of systemically administered analgesics and antiinflammatory drugs. The prognosis for return of vision when acute blindness occurs after trauma is poor. Blindness attributable to optic nerve trauma may be confirmed by a normal electroretinogram in the absence of a direct pupillary light reflex. An electroretinogram should be performed within days of trauma before Wallerian degeneration of the retina occurs.

Chorioretinal degeneration and optic nerve atrophy may result from acute blood loss. Sudden irreversible blindness has been reported following surgical ligation of the internal and external carotid arteries and greater palatine arteries. Ligation of these arteries is one method recommended to treat epistaxis that results from guttural pouch mycosis. Optic nerve ischemia is a risk associated with arterial ligation.

Supplemental Readings

- Brooks DE: Equine ophthalmology. In Gelatt KN (ed): *Veterinary Ophthalmology*, 3rd edition, Baltimore, Lippincott Williams & Wilkins, 1999.
- Brooks DE: Ocular emergencies and trauma. In Auer JA, Stick JA (eds): *Equine Surgery*, 2nd edition, Philadelphia, WB Saunders, 1999.
- Caron JP, Barber SM, Bailey JV et al: Periorbital skull fractures on five horses. *J Am Vet Med Assoc* 1986; 188:280-284.
- Chmielewski NT, Brooks DE, Smith PJ et al: Visual outcome and ocular survival following iris prolapse in the horse: a review of 32 cases. *Equine Vet J* 1997; 29:31-39.
- Lavach JD, Severin GA, Roberts SM: Lacerations of the equine eye: a review of 48 cases. *J Am Vet Med Assoc* 1984; 184:1243-1248.
- Martin L, Kaswan R, Chapman W: Four cases of traumatic optic nerve blindness in the horse. *Equine Vet J* 1986; 18:133-137.

CHAPTER 9.5

Equine Recurrent Uveitis

BRIAN C. GILGER

Raleigh, North Carolina

Equine recurrent uveitis (ERU; also *moon blindness*, *recurring iridocyclitis*, and *periodic ophthalmia*) is a major ophthalmic disease of the horse and the most common cause of blindness in this species. This immune-mediated, panuveitis has approximate prevalence rate of 8% to 25% in horses in the United States. Fortunately, recent advances in the treatment of horses with ERU have led to successful management of this disease. This chapter discusses some important facts about ERU, its causes, and treatment options for the affected horse.

ERU is characterized by episodes of intraocular inflammation that develop weeks to months after an initial episode subsides. However, not every case of initial uveitis in the horse develops into ERU (see later section on diagnosis). Horses can develop ERU at any age, but the peak time of the initial episode is 4 to 6 years, a time when most horses are at or nearing prime performance years.

The equine industry in the United States has an estimated annual worth of \$112 billion and provides approximately 1.4 million full-time jobs across the country. Because ERU has a prevalence rate of approximately 8% to 25% across horse breeds in the United States, the impact of this disease on the equine industry could be as high as a billion dollars a year. ERU causes these large economic losses in the equine industry because it disrupts training, decreases performance, and disqualifies horses from competition (because of medication use, etc.). Furthermore, horses with ERU have decreased value as a result of vision deficits or blindness. Finally, treatment, veterinary care, and personnel costs adds to the economic impact of the disease.

CLINICAL SIGNS

Two main clinical syndromes are observed in ERU—the “classic” and “insidious” type of ERU. Classic ERU is most common and is characterized by active inflammatory episodes in the eye followed by periods of minimal ocular inflammation. The acute, active phase of ERU predominantly involves inflammation of the iris, ciliary body, and choroid, with concurrent involvement of the cornea, aqueous humor, lens, retina, and vitreous. After treatment with nonspecific antiinflammatory medications such as corticosteroids, the signs of active, acute uveitis can recede, and the disease enters a quiescent or chronic phase. After variable periods of time, the quiescent phase is generally followed by further and increasingly severe episodes of uveitis. The recurrent, progressive nature of the disease is responsible for development of cataract, intraocular adhesions, and phthisis bulbi (scarred eye). During the insidious form of ERU, however, the inflamma-

tion never completely resolves, and a low-grade inflammatory response continues that leads to progression of chronic clinical signs of ERU. Affected horses often do not demonstrate overt ocular discomfort, and owners may not recognize the presence of disease until a cataract forms or the eye becomes blind. This type of uveitis is most commonly seen in the Appaloosa and draft breeds.

Typical clinical signs of active ERU are similar to signs of uveitis in other species: photophobia, blepharospasm, corneal edema, aqueous flare, hypopyon, miosis, vitreous haze, and chorioretinitis (Color Plates 6 and 7). Clinical signs of chronic ERU include corneal edema, iris fibrosis and hyperpigmentation, posterior synechia, corpora nigra degeneration (smooth edges), miosis, cataract formation, vitreous degeneration and discoloration, and peripapillary retinal degeneration (Color Plate 8). Either type of ERU (“classic” or “insidious”) can have either predominantly anterior (cornea, iris, lens, and ciliary body inflammation) or predominantly posterior (ciliary body, vitreous, and chorioretinal inflammation) segment involvement. Ultimately, even with aggressive treatment, many horses develop chronic eye pain and blindness as a result of secondary cataract, synechia (intraocular adhesions), scarring, glaucoma, and phthisis bulbi.

ORGANISMS ASSOCIATED WITH INITIAL UVEITIS AND POSSIBLY EQUINE RECURRENT UVEITIS

Several microorganisms have been associated with the initiation of equine uveitis. In some instances, uveitis associated with these systemic infections may develop into immune-mediated uveitis, or ERU. One of the most commonly associated systemic diseases associated with uveitis is leptospirosis. Roberts demonstrated that ERU may develop after primary infection (and acute uveitis) by *Leptospira* sp.; however, ERU typically did not develop until 1 year after the systemic infection. Therefore monitoring the disease by measuring serum titers in horses with documented ERU is not generally beneficial unless a herd or barn outbreak of the uveitis occurs. Onchocerciasis is another systemic disease associated with equine uveitis. Onchocerciasis is much less common since the widespread use of ivermectin; however, it is still a common initiator of uveitis. The inciting cause of uveitis is the inflammatory reaction associated with dead and dying *Onchocerca* microfilaria in the cornea after treatment with an anthelmintic. It is recommended that affected horses be pretreated with systemic antiinflammatory medications (e.g., flunixin meglumine) before use of ivermectin. Treatment with flunixin meglumine for several days after adminis-

Table 9.5-1
Causes of Uveitis in Horses*

Classification	Causes
Trauma	Blunt or penetrating injury
Bacterial organisms	<i>Leptospira</i> organisms <i>Brucella</i> organisms <i>Streptococcus</i> organisms
Viral organisms	Equine influenza Equine viral arteritis Parainfluenza type 3
Parasitic organisms	<i>Onchocerca</i> organisms <i>Strongylus</i> organisms <i>Toxoplasma</i> organisms
Miscellaneous	Endotoxemia Tooth root abscesses Hoof abscesses Neoplasia

*Any injury to a horse's eye may result in uveitis and possibly development of the syndrome of equine recurrent uveitis (ERU). Examples are included in this table.

tration of ivermectin may also be necessary. Other systemic infectious causes of uveitis include *Streptococcus equi* infection, brucellosis, toxoplasmosis, equine herpesvirus-1 and 2 (EHV-1 and -2), equine viral arteritis, parainfluenza type 3, generalized septicemia, endotoxemia, neoplasia, tooth root abscess, or trauma (Table 9.5-1).

PATHOGENESIS OF RECURRENT EPISODES OF UVEITIS

ERU is a nonspecific immune-mediated condition that results in recurrent or persistent inflammatory episodes in ocular tissues. To diagnose the syndrome of ERU, the examiner must differentiate ERU from other causes of uveitis. As mentioned previously, an extensive list of infectious and noninfectious agents may be responsible for initiating acute uveitis in the horse. Although any of these initiating causes of uveitis may allow horses to develop ERU, not all horses with acute uveitis will develop ERU. The recurrent episodes typical of ERU are thought to develop because of one of following three pathogenic mechanisms:

1. An infectious agent or antigen incorporates into the uveal tract after the initial uveitis episode. These inciting antigens become established in the ocular tissues and their continued presence induces periodic episodes of inflammation. Recent reports have suggested that *Leptospira* organisms may be one of the sequestered antigens. However, only 26% to 70% of the eyes had *Leptospira* organisms detected, thus suggesting that other antigens and/or organisms may also play a role in the pathogenesis of the disease.
2. Antibody-antigen complexes deposit into uveal tissues, which incites inflammation at a later time.
3. An immune-competent sensitized T lymphocyte persists in the uveal tract and reactivates when given a

signal. T lymphocytes have been demonstrated to be the predominant infiltrating cell type in chronic ERU eyes and cell-mediated immunity to uveal antigens has been reported in horse with ERU. Studies have revealed that T lymphocytes from eyes with ERU develop an immune mediated inflammation typical of a Th1 inflammatory response (i.e., high interleukin-2 [IL-2], low IL-4 levels). These results strongly suggest a T-cell-mediated autoimmune response in ERU eyes. However, the signal that reactivates these T cells remains unknown. A systemic reexposure to the original antigen, exposure to a self-protein antigen that is similar to the original antigen (i.e., "molecular mimicry"), or a decreased immunologic feedback down-regulation of the T cell could be the inciting signal for reactivation of the T cell and inflammation.

DIAGNOSIS

The clinical diagnosis of ERU is based on the presence of characteristic clinical signs (corneal edema; aqueous flare; posterior synechia; corpora nigra atrophy; cataract formation; vitreous degeneration; retinal edema; or degeneration with or without signs of associated ocular discomfort such as epiphora, periocular swelling, and blepharospasm) and history of documented recurrent or persistent episodes of uveitis. Both features are required to make this clinical diagnosis, specifically to differentiate ERU from non-ERU uveitis and other causes of recurrent or persistent ocular inflammation, such as herpesvirus keratitis or immune-mediated keratitis.

HISTOLOGIC FEATURES

Infiltration of the uveal tract (with the majority of infiltration in the ciliary body and base of the iris) with lymphocytes and macrophages was evident in eyes with chronic ERU. Lymphoid follicles are occasionally present in the base of the iris. Loss of tissue structure/destruction was evident in the ciliary processes. Several distinguishing histologic features of globes with ERU exist: a noncellular hyaline membrane adhered to the inner surface of the nonpigmented ciliary epithelium, linear intracytoplasmic inclusions in the nonpigmented ciliary epithelium, and an influx of lymphocytes and plasma cells into the ciliary body. The choroid also reveals infiltration of mononuclear cells, with overlying retinal degeneration. A previous immunohistochemical study of ERU globes in this author's laboratory revealed infiltration of the uveal tract with lymphocytes, plasma cells, and macrophages that were most evident in the ciliary body and base of the iris. Loss of tissue structure (destruction) was most evident in the ciliary processes. Infiltrating lymphocytes were predominantly CD 4+ T cells (e.g., 48% CD4+ and 18% CD8+ in the ciliary body stroma), as determined by immunohistochemistry. Few inflammatory cells were observed in normal eyes.

TREATMENT

The main goals of treatment for ERU are to preserve vision and reduce and control ocular inflammation in an attempt to limit permanent damage to the eye. When a

definitive inciting cause has been identified, treatment is directed at eliminating the primary problem, and initial tests to isolate an inciting agent are performed. These tests may consist of a complete blood count, serum biochemical analysis, conjunctival biopsy, and serologic titers for bacterial and viral agents. More often, however, one particular cause cannot be identified. In these instances, therapy is directed at the alleviating clinical signs and reducing ocular inflammation.

Management Practices to Decrease the Incidence of Equine Recurrent Uveitis

Practices that decrease ocular injury or minimize the inflammatory stimuli may decrease or eliminate the development of recurrent episodes of uveitis in ERU (Table 9.5-2). It may be possible to eliminate environmental triggers (e.g., allergens, antigens, etc.) of the recurrent episodes of uveitis by changing the horses' pasture, pasture mates, or stable, increasing insect and rodent control, decreasing sun exposure, or changing bedding type. Trauma to the eye(s) can also be decreased by eliminating sharp edges, nails, and hooks in the stable, removing low tree branches in the pasture, reducing training and show schedule, minimizing trailering, and consistently using a quality fly mask. Finally, ensuring that the horse has proper hoof care, optimal vaccination and anthelmintic schedule, and proper diet may also minimize uveitis episodes.

Medical Therapy

Because vision loss is a common long-term consequence of ERU, initial therapy must be immediate and aggressive. In acute active ERU, treatment in the form of systemic and local therapy that consists of antibiotics, corticosteroids, and antiinflammatory drugs is used, often simultaneously (Table 9.5-3). Initial therapy is instituted for at least two weeks, and treatment should be reduced slowly over an additional two weeks after the resolution of clinical signs. In severe ERU, local subconjunctival injections of corticosteroids may be indicated as an adjunct to topical and systemic therapy. In most instances, a subpalpebral lavage catheter is placed to facilitate delivery of topical medications (see Chapter 9.3: "Ocular Therapy"). Many horses respond well to intermittent topical and/or systemic therapy of their active episodes of ERU. Other horses, however, do not respond to traditional therapy and may experience frequent recurrences of uveitis.

Traditional treatments used for ERU (i.e., corticosteroids and nonsteroidal antiinflammatory medications) are aimed at reducing inflammation and minimizing permanent ocular damage at each active episode. They are not effective in preventing recurrence of disease. Other medications used to prevent or decrease severity of recurrent episodes—such as aspirin, phenylbutazone, and various herbal treatments—have limited efficacy and potential detrimental effects on the gastrointestinal and hematologic systems when used chronically in the horse. Two recently described surgical procedures, intravitreal cyclosporine A devices (IVC-As) and core vitrectomy (CV), are aimed at preventing the recurrence of uveitis and therefore provide long-term control of the disease.

Table 9.5-2

Practices to Decrease Equine Recurrent Uveitis

Classification	Practice to Institute
Environmental	Change pasture/stable/pasture mates. Increase insect and rodent control. Decrease dust. Decrease sun exposure. Change bedding type.
Health maintenance	Perform proper hoof and dental care. Institute an optimal anthelmintic and vaccination schedule. Maintain proper diet.
Decrease in ocular trauma	Minimize weeds in pasture. Eliminate sharp objects in stable. Eliminate low tree branches in pasture. Decrease training and show schedule. Minimize trailering. Do not feed from hay nets. Use quality fly mask.

Intravitreal Cyclosporine A

A polyvinyl alcohol/silicone-coated IVC-A sustained-delivery device that has been shown previously to produce a sustained level of cyclosporine A (CsA) in ocular tissues of the rabbit was evaluated for use in horses (Figure 9.5-1 and Color Plate 9). A CsA device was implanted into normal horse eyes for up to 1 year and was not associated with ocular inflammation or complications. In equine eyes with experimentally induced uveitis, the IVC-As decreased the duration and severity of inflammation, cellular infiltration, tissue destruction, and level of transcription of proinflammatory cytokines. This 2-mm × 3-mm device releases 4 µg/day of CsA when placed into the vitreous through a full-thickness scleral and pars plana incision and anchored into place by suturing the stem of the device into the scleral incision (Figure 9.5-1 and Color Plate 9). The estimated time that the device will continue to deliver medication is 5 years.

In a recent study of IVC-As in horses with naturally occurring ERU, horses that experienced frequent recurrence of uveitis without vision-threatening ocular changes (i.e., cataracts, retinal degeneration) or systemic illnesses were selected to receive the device. Few complications occurred during and after surgery. Only 2 of 16 horses had severe complications that resulted in vision loss after surgery. One horse developed retinal detachment, and one developed a mature cataract. Few recurrent episodes of uveitis were noted; only 3 (19%) developed any evidence of uveitis after device implantation. Vision was judged to be normal in 14 of 16 horses (88%) at a mean follow-up of 13.8 months (range 6-4 months).

Core Vitrectomy

Few publications in English have described this surgical technique, but several abstracts and articles in the German

Table 9.5-3
Medical Therapy for Equine Recurrent Uveitis

Medications	Dose	Indication	Caution
Topical Medications			
prednisolone acetate 1%	q1-6h	Potent antiinflammatory drug with excellent ocular penetration	Predisposes to corneal fungal infection
dexamethasone HCl 0.05%-0.1%	q1-6h	Potent antiinflammatory drug with excellent ocular penetration	Predisposes to corneal fungal infection
flurbiprofen, voltaren, (or other topical NSAIDs)	q1-6h	NSAIDs with good ocular penetration	Decreases corneal epithelialization
cyclosporine A 0.02%-2%	q6-12h	Strong immunosuppressive drug	Poor eye penetration; weak antiinflammatory effect
atropine HCl 0.5%-1%	q6-48h	Cycloplegic, mydriatics (pain relief and minimization of synechia formation)	May decrease gut motility and predispose to colic
Systemic Medications			
flunixin meglumine	0.5 mg/kg PO, IV, or IM for 5 days then 0.25 mg/kg PO	Potent ocular antiinflammatory drug	Long-term use may predispose to gastric and renal toxicity.
phenylbutazone	4.4 mg/kg PO or IV	Antiinflammatory medication	Long-term use may predispose to gastric and renal toxicity.
prednisolone	100-300 mg/day PO or IM	Potent antiinflammatory medication	Frequent side effects; laminitis formation (used with caution and only as a last resort). Must taper off dose.
dexamethasone	5-10 mg/day PO or 2.5-5 mg daily IM	Potent antiinflammatory medication	Frequent side effects; laminitis formation (used with caution and only as a last resort). Must taper off dose.
subconjunctival triamcinolone	1-2 mg	Repositol; potent antiinflammatory medication with a duration of action of 7-10 days	Severe predisposition for bacterial or fungal keratitis; cannot remove therapy once given

q1-6h, Every 1 to 6 hours; NSAID, nonsteroidal antiinflammatory drug; PO, by mouth; IV, intravenous; IM, intramuscular.

veterinary literature describe results of this surgery. This surgery uses a single-port, nearly total vitrectomy, in which an incision is made 1 cm posterior to the dorsolateral limbus, through the pars plana, and into the vitreous. The vitreous is removed and is replaced by saline or balanced salt solution. Removal of T cells or organisms from the vitreous is the goal and is thought to decrease the recurrent episodes of uveitis. In fact, the surgery reportedly decreases ERU recurrence by 92%. However, the goal of this surgery is to arrest the progression and recurrent episodes of uveitis, not necessarily to preserve vision. In one study, approximately one third of affected eyes were deemed blind months after surgery, and the study's authors observed a decrease in vision despite a decrease in recurrent episodes. This may be attributable to an exceedingly high rate of cataract formation after surgery. In the only English publication of this surgical technique in which horses were reexamined by the surgeons, 12 of 27 (45%) horses had "significant" cataract formation. This

surgical technique was recommended to help preserve vision (but not to increase vision), decrease recurrent episodes, and to avoid enucleation. Studies of CV done in the United States indicate that a high percentage of cataract formation after surgery and that most horses have decreased vision; however, the episodes of uveitis appeared to decrease.

Both IVC-As and CV are being evaluated at several centers in the United States for long-term control of ERU. Six sites across the United States are currently performing the IVC-As procedure, but all ophthalmologists with facilities for equine ocular microsurgery could perform this surgery. Fewer locations are currently performing CV in the United States, including the University of Florida and North Carolina State University. Table 9.5-4 provides a comparison of CV and IVC-As surgical techniques.

Selection of appropriate horses to receive the IVC-As device or CV is very important for long-term success after surgery. Chronic uveitic changes in the eye—such as

Figure 9.5-1 Location of a cyclosporine A intravitreal implant device in the eye.

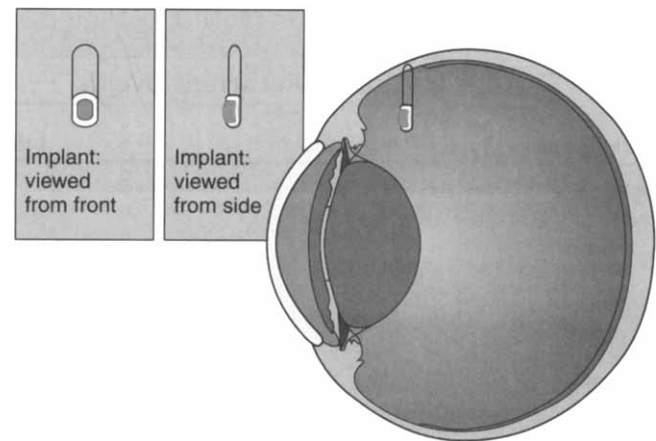


Table 9.5-4
Comparison of Surgical Techniques for Equine Recurrent Uveitis

	Core Vitrectomy	Intravitreal Cyclosporine A
Stage of ERU	Progressive, posterior, chronic	Progressive, anterior or posterior, minimal ocular changes
Surgical Procedure		
General anesthesia?	Yes	Yes
Specialized surgical equipment?	Yes—vitrectomy unit modified for use in horses	No—standard microsurgery/ophthalmic instrumentation
Length of procedure	Extensive, long	Simple, short
Number of horses treated	500-1000 in Europe Less than 100 in United States	Less than 100
Long-term results	Good control of recurrent episodes, significant cataract formation in 40%-45%	Excellent (88%)
Potential for blinding complications?	Yes	Yes
Cost	Approximately \$3000-\$4000	Approximately \$1500
Availability	Not widely available in the United States (UF, NCSU currently performing the procedure)	Limited, device not commercially available (approximately 6 sites performing the procedure throughout the United States)

UF, University of Florida; NCSU, North Carolina State University.

synechiae, corneal edema, glaucoma, vitreal degeneration, and retinal atrophy—will decrease vision in the eye and decrease the long-term success of the IVC-As because these changes cannot be reversed. Eyes with cataract should be excluded as candidates for implantation. In a previous study of a 2 μ g/day-release CsA device in horses, cataracts that involved approximately 25% of the lens or more continued to progress despite the fact that recurrent episodes of inflammation were largely eliminated. Cataract formation is even more common after CV; nearly 45% of cases that were followed developed significant cataract formation.

The goal of both IVC-As and CV is to prevent further inflammatory episodes and thereby prevent additional chronic damage to eyes. Eyes with less chronic changes

are more suitable candidates for IVC-As surgery with a 4 μ g/day device because these vision-threatening complications may be prevented. However, eyes with more chronic changes and significant cataract formation (>25% of the lens) may be better candidates for CV. With chronic changes in the eyes (i.e., cataract formation, posterior synechia, retinal degeneration), CV may not return or preserve vision but may decrease the number and severity of recurrent episodes of uveitis, thereby maintaining comfort of the eye and eliminating the need for enucleation.

IVC-As and CV are relatively new treatments for long-term control of ERU. IVC-As are indicated for eyes with progressive ERU but minimal ocular changes. CV is recommended for predominantly posterior ERU and in eyes with

significant ocular changes (i.e., synechiae, cataract, vitreal degeneration, and retinal atrophy) in advanced-stage ERU.

Supplemental Readings

Davidson MG: Anterior uveitis. In Robinson NE (ed): *Current Therapy in Equine Medicine*, 3rd edition, pp 593-594, Philadelphia, WB Saunders, 1992.

Faber N, Crawford M, LeFebvre R et al: Detection of *Leptospira* spp. in the aqueous humor of horses with naturally acquired recurrent uveitis. *J Clin Microbiol* 2000; 38:2731-2733.

Fruhauf B, Ohnsesorge B, Deegen E et al: Surgical management of equine recurrent uveitis with single port pars plana vitrectomy. *Vet Ophthalmol* 1998; 1:137-151.

Gilger BC, Malok E, Cutter KV et al: Characterization of T-lymphocytes in the anterior uvea of eyes with chronic equine recurrent uveitis. *Vet Immunol Immunopathol* 1999; 71:17-28.

Gilger BC, Wilkie DW, Ashton P et al: Intravitreal cyclosporine (CsA) implants in horses with naturally-occurring recurrent uveitis [abstract]. *Invest Ophthalmol Vis Sci* 2000; 41(Suppl):380.

CHAPTER 9.6

Ocular Manifestations of Equine Herpesviruses

DAVID J. MAGGS
Davis, California

Herpesviruses cause upper respiratory and ocular signs in most host species studied to date. Although many of the equine herpesviruses have been incriminated as ocular pathogens, little is known about their true role in ocular disease; much of the information that exists is anecdotal or based on response to treatment. Clinical signs attributable to herpesvirus diseases often wax and wane sporadically; therefore response to treatment as the basis for diagnosis is particularly unreliable. Compounded by additional difficulty in obtaining laboratory confirmation of equine herpesviruses, the equine practitioner is confronted by a number of dilemmas. Until contemporary laboratory and clinical research provide definitive and reliable results favoring the diagnosis, the equine practitioner is forced to extrapolate knowledge established for herpesviruses in other species and apply it to the horse.

To date, five genetically distinct equine herpesviruses (EHV) have been identified (EHV-1 through EHV-5). Use of more highly accurate molecular techniques has made it apparent that some of the previous reports did not adequately differentiate between EHV-1 and -4, both of which were considered subtypes of EHV-1, or between EHV-2 and -5. Therefore interpretation of scientific study results reported previously is often difficult and unreliable.

OCULAR MANIFESTATIONS OF EQUINE HERPESVIRUSES

The following section contains a description of ocular signs attributable to equine herpesviruses. The format is

designed for use as an easy reference by the equine practitioner presented with a horse exhibiting one or more of the ocular manifestations of equine herpesviruses. Clinical signs suggestive of herpetic involvement, along with potential differential considerations, diagnostic tests, and treatments, are described. Because currently available laboratory tests are of limited value in confirming a diagnosis of equine herpesvirus, the emphasis is on *clinical* methods of diagnosis. The most important reason for this is the frequency with which equine herpesviruses (or serum antibody titers to equine herpesviruses) may be detected in clinically normal horses.

Ocular signs associated with or attributable to equine herpesviruses may be divided into two broad categories: (1) primary ocular disease in the absence of systemic signs (e.g., primary keratoconjunctivitis attributable to EHV-2 infection); and (2) ocular signs as a component of a major systemic syndrome (e.g., conjunctivitis and concurrent respiratory disease; Box 9.6-1).

Conjunctivitis

Clinical Signs

Herpetic conjunctivitis occurs as part of the respiratory syndrome reported with EHV-1 and -4 and separately or associated with keratitis in horses infected with EHV-2. Clinical signs of conjunctivitis associated with EHV-1, -2, and -4 include serous ocular discharge that becomes mucopurulent as clinical signs persist, chemosis, and conjunctival hyperemia. Ocular signs are not pathognomonic for the herpesviruses or for a genetically specific type of EHV. Therefore diagnostic emphasis is placed on the (1) presence or absence of accompanying clinical signs; and (2) elimination of other known causes of conjunctivitis in the horse.

significant ocular changes (i.e., synechiae, cataract, vitreal degeneration, and retinal atrophy) in advanced-stage ERU.

Supplemental Readings

Davidson MG: Anterior uveitis. In Robinson NE (ed): *Current Therapy in Equine Medicine*, 3rd edition, pp 593-594, Philadelphia, WB Saunders, 1992.

Faber N, Crawford M, LeFebvre R et al: Detection of *Leptospira* spp. in the aqueous humor of horses with naturally acquired recurrent uveitis. *J Clin Microbiol* 2000; 38:2731-2733.

Fruhauf B, Ohnsesorge B, Deegen E et al: Surgical management of equine recurrent uveitis with single port pars plana vitrectomy. *Vet Ophthalmol* 1998; 1:137-151.

Gilger BC, Malok E, Cutter KV et al: Characterization of T-lymphocytes in the anterior uvea of eyes with chronic equine recurrent uveitis. *Vet Immunol Immunopathol* 1999; 71:17-28.

Gilger BC, Wilkie DW, Ashton P et al: Intravitreal cyclosporine (CsA) implants in horses with naturally-occurring recurrent uveitis [abstract]. *Invest Ophthalmol Vis Sci* 2000; 41(Suppl):380.

CHAPTER 9.6

Ocular Manifestations of Equine Herpesviruses

DAVID J. MAGGS
Davis, California

Herpesviruses cause upper respiratory and ocular signs in most host species studied to date. Although many of the equine herpesviruses have been incriminated as ocular pathogens, little is known about their true role in ocular disease; much of the information that exists is anecdotal or based on response to treatment. Clinical signs attributable to herpesvirus diseases often wax and wane sporadically; therefore response to treatment as the basis for diagnosis is particularly unreliable. Compounded by additional difficulty in obtaining laboratory confirmation of equine herpesviruses, the equine practitioner is confronted by a number of dilemmas. Until contemporary laboratory and clinical research provide definitive and reliable results favoring the diagnosis, the equine practitioner is forced to extrapolate knowledge established for herpesviruses in other species and apply it to the horse.

To date, five genetically distinct equine herpesviruses (EHV) have been identified (EHV-1 through EHV-5). Use of more highly accurate molecular techniques has made it apparent that some of the previous reports did not adequately differentiate between EHV-1 and -4, both of which were considered subtypes of EHV-1, or between EHV-2 and -5. Therefore interpretation of scientific study results reported previously is often difficult and unreliable.

OCULAR MANIFESTATIONS OF EQUINE HERPESVIRUSES

The following section contains a description of ocular signs attributable to equine herpesviruses. The format is

designed for use as an easy reference by the equine practitioner presented with a horse exhibiting one or more of the ocular manifestations of equine herpesviruses. Clinical signs suggestive of herpetic involvement, along with potential differential considerations, diagnostic tests, and treatments, are described. Because currently available laboratory tests are of limited value in confirming a diagnosis of equine herpesvirus, the emphasis is on *clinical* methods of diagnosis. The most important reason for this is the frequency with which equine herpesviruses (or serum antibody titers to equine herpesviruses) may be detected in clinically normal horses.

Ocular signs associated with or attributable to equine herpesviruses may be divided into two broad categories: (1) primary ocular disease in the absence of systemic signs (e.g., primary keratoconjunctivitis attributable to EHV-2 infection); and (2) ocular signs as a component of a major systemic syndrome (e.g., conjunctivitis and concurrent respiratory disease; Box 9.6-1).

Conjunctivitis

Clinical Signs

Herpetic conjunctivitis occurs as part of the respiratory syndrome reported with EHV-1 and -4 and separately or associated with keratitis in horses infected with EHV-2. Clinical signs of conjunctivitis associated with EHV-1, -2, and -4 include serous ocular discharge that becomes mucopurulent as clinical signs persist, chemosis, and conjunctival hyperemia. Ocular signs are not pathognomonic for the herpesviruses or for a genetically specific type of EHV. Therefore diagnostic emphasis is placed on the (1) presence or absence of accompanying clinical signs; and (2) elimination of other known causes of conjunctivitis in the horse.

BOX 9.6-1**Clinically Important Equine Herpesviruses and Associated Major Clinical Syndromes*****EHV-1 (Equine Abortion Virus)**

Abortion and perinatal mortality

Neurologic disease

Nystagmus

Blindness

Strabismus

Facial paralysis

Ptosis

Keratoconjunctivitis sicca

Exposure keratitis

Retinal hemorrhage

Optic neuritis

Respiratory disease

Transient mild conjunctivitis

? Delayed onset chorioretinitis

? Anterior uveitis

Immunosuppression

Respiratory disease

Poor performance syndrome

EHV-3 (Equine Coital Exanthema Virus)

Pustular vaginitis

Vulvitis

Balanoposthitis

EHV-4 (Equine Rhinopneumonitis Virus)

Respiratory disease

Transient mild conjunctivitis

Abortion

EHV-5

? Respiratory disease

EHV-2 (Equine Cytomegalovirus)

Conjunctivitis

Superficial keratitis

Ulcerative

Nonulcerative

? = Causal association has not been proven; *EHV*, equine herpesvirus.

*Where relevant, ocular manifestations of each syndrome are listed.

Bilateral conjunctivitis attributable to EHV-1 or -4 is usually a relatively inconspicuous clinical sign specifically when overshadowed by substantial signs of concurrent respiratory infection. Characteristic features associated with respiratory disease that make conjunctivitis less conspicuous include fever, inappetence, pharyngitis, nasal discharge, lymphadenopathy, and occasional cough. Younger horses, particularly yearlings, are more severely affected, although mature horses are believed to shed the virus subclinically. Sporadic abortions may also occur with either virus, and abortion storms have been reported with EHV-1. Conjunctivitis may be the only clinical sign attributable to EHV-2 infection; however, concurrent keratitis more commonly is a more prominent clinical sign (Color Plate 10).

Differential Diagnosis and Diagnostic Testing

Horses with conjunctivitis should be assessed for concurrent signs of systemic disease. Owners should also be questioned about the health of other horses in contact with an affected horse. Because other ocular diagnoses such as keratitis, iridocyclitis, and secondary glaucoma may initiate conjunctival hyperemia, a thorough ocular examination is always recommended. Eyes should be examined with distant retroillumination, and pupil size and symmetry should be compared to assess clarity of the cornea, aqueous humor, crystalline lens, and vitreous humor. This assessment is best performed in a darkened room with a focal light source such as a Finoff transilluminator or direct ophthalmoscope held close to the examiner's eye and at least an arm's distance from the eye. Tapetal reflections are then

used to compare pupil size between eyes. Conjunctival hyperemia and a constricted pupil suggest iridocyclitis or the oculopupillary reflex associated with corneal or conjunctival irritation or inflammation, whereas conjunctival hyperemia and a dilated pupil may suggest glaucoma. Subtle superficial corneal lesions, as seen with EHV-2 keratitis, are also more easily identified when retroillumination is used (see Color Plate 10). Further information regarding likely causes of conjunctival hyperemia may be gained by evaluating for presence of aqueous flare (pathognomonic for iridocyclitis), measuring intraocular pressure (elevated in glaucoma and reduced in iridocyclitis) and tear production by Schirmer tear test, and topically applying fluorescein sodium or rose bengal dyes.

Differential diagnoses include viral (equine adenovirus, equine influenza, equine viral arteritis), parasitic (*Thelazia*, *Habronema*, *Onchocerca* organisms), bacterial (rarely primary), allergic or immune-mediated disease (eosinophilic, lymphocytic-plasmacytic), keratoconjunctivitis sicca (KCS), foreign body, neoplastic (squamous cell carcinoma, lymphosarcoma, hemangiosarcoma), and, infrequently, fungal conjunctivitis. Collection of conjunctival tissue by conjunctival scraping or "snip" biopsy after sedation and application of a topical anesthetic is recommended. Samples may be examined cytologically or histologically and may be submitted for viral, bacterial, and sometimes fungal culture. Serologic testing may be useful for assessment of EHV-1 or -4, specifically in an outbreak; however, they are not useful for diagnosing EHV-2 because of the endemic nature of EHV-2 in the horse population.

Topical Ocular Treatment

Conjunctivitis associated with respiratory syndromes in horses is usually mild and self-limiting, and treatment is usually not necessary. Occasionally, prevention of bacterial overgrowth may be considered. A broad-spectrum ophthalmic antibiotic preparation (such as neomycin-polymyxin-gramicidin) that does not contain a corticosteroid can be administered 2 or 3 times daily. An ointment is more easily applied and has the added advantage of longer contact time. In many instances, response to treatment with only a lubricant ointment is equally as good. Topical antiviral drugs are not recommended in horses with conjunctivitis unless concurrent keratitis is evident. Use of topical corticosteroid preparations is contraindicated because they often exacerbate herpesvirus keratoconjunctivitis even though they may result in apparent improvement in clinical signs because of their antiinflammatory effects. Topical corticosteroid drugs cause viral reactivation, slow the rate of healing, and may favor or exacerbate corneal ulceration.

Keratitis

Clinical Signs

Herpetic keratitis attributable to replication of virus in ocular tissues has been associated with EHV-2 only. Keratitis secondary to EHV-1 myeloencephalitis is attributable to neurologic dysfunction and is described in the following section. Keratitis attributable to EHV-2 may occur in individual horses or as small outbreaks, especially in young horses, and recurrences are common. Diagnosis of EHV-2 keratitis is reported more often in Britain than in other countries, but the reason for this is unclear. Ulcerative and nonulcerative keratitis have been reported; however, they may represent different stages of the same disease. Affected horses are usually first identified when severe unilateral epiphora and blepharospasm occur with rapid onset. Close inspection reveals variable corneal opacity, iridocyclitis, and/or conjunctivitis. Various patterns of corneal opacification and/or ulceration have been described: (1) multifocal, circular to ring-shaped lesions scattered irregularly across the corneal surface; (2) generalized epithelial irregularity causing a stippling or "orange-peel" appearance; and (3) reticulated or lacelike (dendritic) networks of linear opacities in the anterior stroma.

The best technique for identifying these subtle corneal lesions is retroillumination (see Color Plate 10). Variable corneal stromal inflammatory cell infiltration, edema, and neovascularization have been described in association with epithelial disease attributable to EHV-2. Concurrent conjunctivitis is often detected. However, unlike conjunctivitis attributable to EHV-1 or -4, EHV-2 keratoconjunctivitis most commonly occurs unilaterally, and concurrent respiratory signs are usually absent or mild. Clinical signs of iridocyclitis associated with EHV-2 are typically inconspicuous and may manifest as a miotic pupil and absence of aqueous flare or cell.

Differential Diagnoses and Diagnostic Testing

The clinical appearance of herpetic keratitis has been described as characteristic and diagnostic of the disease. However, a case series of superficial ulcers with strikingly similar clinical appearances and from which fungal organisms

were identified has been reported. Additionally, because laboratory confirmation of EHV-2 is problematic, efforts should be directed toward eliminating other infectious causes, particularly fungal organisms. Clinical examination should include retroillumination, Schirmer tear tests, direct examination of corneal defects with magnification and a focal light source, and application of fluorescein sodium and rose bengal dyes (see Chapter 9.1: "Examination of the Eye"). Rose bengal- and fluorescein-retaining herpetic lesions may be overlooked unless magnification is used. Corneal scrapings should be collected from an affected eye after the horse is chemically sedated and topical anesthetic has been instilled. Epithelial cells collected by corneal scrapings should be examined cytologically and submitted for viral, fungal, and bacterial culture. Rose bengal and fluorescein sodium dyes are known to inhibit growth of other closely related herpesviruses; therefore samples for viral isolation should be collected before application of vital dyes. Serologic assays are not useful because of the endemic nature of EHV-2. Interpretation of viral isolation is also of questionable diagnostic value because EHV-2 may be detected in the conjunctival fornix of normal horses.

Ocular Treatment

Although no topical antiviral drugs are labeled for use in horses, some have been used with success to treat herpetic keratitis in horses. These drugs have undergone little scientific scrutiny with respect to efficacy against equine herpesviruses, particularly EHV-2. Therefore anticipated efficacy and frequency of application are usually extrapolated from data generated from their use in other species. Some general comments are likely to apply to horses and equine herpesviruses. Antiviral drugs that are currently available are virostatic and therefore should be applied frequently. The treatment regimen recommended for humans (q2h administration) is usually not possible in horses. However, administration at frequent intervals is recommended, and therapy should be initiated early in the course of the disease. For most antiviral drugs, administration should occur a minimum of every 6 hours. Antiviral drugs tend to be relatively toxic to corneal and conjunctival epithelium, and clinical signs consistent with toxicity include apparent irritation when medications are administered and delayed healing of ulcers and erosions.

Most clinical reports describe topical administration of idoxuridine or trifluridine for treatment of equine herpetic keratitis. In other species studied, trifluridine had corneal penetration superior to other antiviral drugs. Although this may be advantageous in nonulcerative herpetic keratitis, it is probably of little relevance in ulcerative disease. In cats, trifluridine also appears to be more poorly tolerated than other topical antiviral drugs because of surface irritation. However, this has not been described as an adverse side effect after topical administration in horses. Finally, trifluridine drug is available commercially in the United States as a 1% ophthalmic solution only, and administration of topical ocular solutions to eyes of horses may be problematic. Idoxuridine is no longer commercially available in the United States; however, it can be compounded as an ophthalmic ointment (0.5%) or solution (0.1%) and appears clinically efficacious and well tolerated in equine herpetic keratitis. Vidarabine is commercially available as a 3% ophthalmic ointment,

appears to be well tolerated, and has relatively low epithelial toxicity in comparison to trifluridine and idoxuridine. Its efficacy against equine herpesviruses is unknown, but anecdotal reports suggest it is effective. Acyclovir has been shown to have unreliable *in vitro* efficacy against EHV-1, is moderately toxic to other species tested, and is not available as an ophthalmic preparation in the United States. This author does not recommend use of acyclovir for EHV keratitis when relatively safe alternative topical antiviral drugs are available. Modern antiviral drugs such as ganciclovir and penciclovir have shown reasonable antiviral action against EHV-1 and EHV-3 *in vitro* and may hold some promise for ophthalmic use. Antiviral drugs do not have antibacterial properties; therefore horses with ulcerative keratitis should also be treated concurrently with a topical antibiotic drug.

Treatment with corticosteroids is contraindicated when ulcerative keratitis is present and when active herpetic disease is evident or suspected. Treatment with corticosteroids may exacerbate or reactivate herpetic keratitis in horses. For these reasons, topically or systemically administered corticosteroids should be avoided in horses with herpetic keratitis. Use of topical nonsteroidal antiinflammatory drugs may also exacerbate herpetic keratitis and should also be avoided.

Anterior uveitis often occurs with herpetic keratitis and is a substantial component of ocular pain. Anterior uveitis usually responds to topical atropine ophthalmic ointment that is applied as often as necessary to achieve and then maintain wide pupil dilation. Often only once- or twice-weekly application is required.

Ocular Signs Secondary to Neurologic Disease

Clinical Signs and Diagnostic Testing

More noticeable clinical signs of myeloencephalitis often overshadow ocular signs of EHV-1. However, equine practitioners should be aware of ocular signs, examine eyes of horses for their presence, and institute treatment when needed. Nystagmus, blindness, strabismus, ptosis, exposure keratitis, KCS, optic neuritis, and retinal hemorrhage have been reported in horses with EHV-1 myeloencephalitis. Ocular signs represent manifestations of central nervous system (CNS) or peripheral cranial nerve disease.

The cause of exposure keratitis is presumed to be trigeminal (cranial nerve [CN] V) and/or facial (CN VII) nerve dysfunction with resultant inability to sense corneal dryness, stimulate tear production by the lacrimal gland, and/or blink. Clinical signs of exposure keratitis include a dry, lackluster corneal surface, and occasionally secondary corneal ulceration or superficial neovascularization and concurrent conjunctivitis. Corneal and facial sensitivity and eyelid function should be evaluated. Corneal sensitivity may be evaluated crudely by lightly brushing the corneal surface with the end of a cotton-tipped applicator after teasing a few fibers to a soft point. This should elicit a strong blink reflex. Gentle tapping of the eyelids with a finger should also elicit a blink reflex. In normal horses, stimulating the medial canthal region produces a more marked blink. A weak or absent blink reflex may be seen with CN V or VII dysfunction. Marked globe retraction and third eyelid protrusion may occur after eyelid or corneal stimulation with CN VII dysfunction but normal CN V function. Schirmer tear tests and application of flu-

orescein sodium and possibly rose bengal dyes should also be done initially and to monitor the disease progress.

Ocular Treatment

Ptosis, strabismus, nystagmus, blindness, optic neuritis, and retinal hemorrhage do not require specific ocular treatment. Systemically administered antiinflammatory drugs should be used to treat neuritis or vasculitis when evident. However, exposure keratitis and KCS, which may be seen unaccompanied or simultaneously in the same animal, require specific ocular treatment. Frequent (at least 4× daily) application of a lubricant or antibiotic ophthalmic ointment is recommended when exposure keratitis and/or KCS is mild. Corticosteroid drug-containing ointments should not be used. Topical application of cyclosporine ophthalmic ointment twice daily may stimulate tear production and is safe even when corneal ulceration is present but may exacerbate corneal epithelial disease attributable to EHV-1. Horses with marked keratitis should have a partial, lateral, temporary tarsorrhaphy placed to protect the cornea. Lateral placement leaves exposed a small area of cornea medially through which the horse can see, corneal health can be monitored, and topical ocular medications can be administered. The third eyelid in this region protects the cornea. Assessment of returning nerve function can be assessed clinically with palpebral and corneal reflexes even with a partial temporary tarsorrhaphy.

Anterior Uveitis/Chorioretinitis

Anterior uveitis and chorioretinitis have been reported in horses with spontaneously occurring or experimentally induced EHV-1 infection. However, an exact causal association remains undefined. In one report, a foal that was experimentally infected with EHV-1 developed classic respiratory signs and recovered spontaneously. Approximately one month later, the foal had severe vision impairment evident clinically as absent bilateral menace responses, dilated pupils, sluggish pupillary light reflexes, asymmetric optic nerve heads, and retinal degeneration with altered fundic pigmentation. Iridocyclitis was not detected. A separate report described an outbreak of neurologic disease and neonatal mortality attributed to EHV-1 in which a number of affected foals also had clinical signs of iridocyclitis. Clinical signs included self-limiting hypopyon and blindness. In both reports, iridocyclitis may have been a manifestation of generalized vasculitis or may have been attributable to superinfection caused by a more specific uveal pathogen secondary to EHV-1-mediated immunosuppression.

Supplemental Readings

- Collinson PN, O'Reilly JL, Ficorilli N et al: Isolation of equine herpesvirus type 2 (equine gammaherpesvirus 2) from foals with keratoconjunctivitis. *J Am Vet Med Assoc* 1994; 205:329-331.
- Donaldson MT, Sweeney CR: Herpesvirus myeloencephalopathy in horses: 11 cases (1982-1996). *J Am Vet Med Assoc* 1998; 213:671-675.
- Matthews AG, Handscombe MC: Superficial keratitis in the horse: treatment with the antiviral drug idoxuridine. *Equine Vet J* 1983; 2(Suppl):29-31.
- Miller TR, Gaskin JM, Whitley RD et al: Herpetic keratitis in a horse. *Equine Vet J* 1990; 10(Suppl):15-17.

CHAPTER 9.7

Fungal Keratitis

STACY E. ANDREW

Gainesville, Florida

Mold, yeast, and fungi are considered normal surface resident flora of the equine conjunctiva and cornea. Fungal organisms reported most frequently include *Aspergillus*, *Penicillium*, *Alternaria*, *Cladosporium*, *Fusarium*, *Geotrichum*, and *Candida*, and fungal growth in culture has been reported in up to 95% of normal horses. The type of fungi isolated from the normal equine eye varies by geographic region of the country as well as season of the year. The majority of fungal organisms is considered to be saprophytic but may become opportunistic pathogens after corneal injury or alteration of the normal resident bacterial flora by, for example, topical antibiotics. Because horses have large eyes and live in environments in which fungi are ubiquitous, more isolation of fungal organisms from healthy and diseased corneas occurs in equine eyes than in eyes of other species.

The corneal and conjunctival surface epithelia form the most important and effective barrier to ocular infection by opportunistic microorganisms. Eyelids, tear lysozymes, β lysin, lactoferrin, secretory immunoglobulins, and tear film leukocytes also provide corneal protection. Resident microbial flora assist in maintaining ocular surface health by restricting nutrients to potentially pathogenic microbes, occupying surface space, and secreting inhibitory substances. The resident microbial flora produce substances such as polypeptide antibiotics that have antibacterial and antifungal properties that moderate the growth of opportunistic pathogenic organisms and transient flora of the ocular surface and therefore restrict fungal growth. Topical treatment with antibiotics or corticosteroids may alter the microbial flora and result in an environment more suitable for fungal colonization. Microbial population dynamics are often altered in diseased ocular states or after topical or systemic administration of antimicrobial or corticosteroid drugs. Subsequently, microbial overgrowth by resident flora or alterations in microbial populations by pathogenic organisms may occur. For example, in horses a positive correlation exists between long-term topical use of ophthalmic antibiotic or corticosteroid drugs and fungal keratitis. Topically applied antibiotics suppress resident ocular flora and subsequently their production of polypeptide antibiotics that would normally retard growth of resident opportunistic fungal organisms. Use of topical corticosteroid drugs has been documented to enhance fungal replication and limit efficacy of antifungal medications.

In studies concerned with normal resident microbial populations of the ocular surface, a number of factors appear to influence the prevalence of individual microorganisms—including geography, climate, season, species, sampling and culturing techniques, and immediate envi-

ronment. Horses with fungal keratitis often have a history of corneal trauma. Owners may have initiated topical treatment with antibiotics or, less often, with corticosteroids. When the corneal epithelium is absent, fungal organisms may adhere to corneal stroma, infiltrate, and multiply, thereby resulting in fungal keratitis. Deep fungal keratitis does not necessarily represent inoculation of the deep stroma by fungal organisms. Although any level of the corneal stroma may be the site of keratomycosis, the trend is for superficial mycoses to progress deep in the stroma with chronicity. This may occur for two reasons. First, fungal growth is typified by “tip” elongation—hyphal tips may grow toward the deep stroma in an attempt to escape host natural immunity responses of the ocular surface. Second, fungi prefer an environment rich in glycosaminoglycans (GAGs) for optimal growth. Stroma directly adjacent to Descemet’s membrane (the basement membrane of the corneal endothelium) has greater amounts of GAGs than do the superficial or intermediate levels of the stroma. The histological appearance of numerous fungal hyphae deep in the stroma and directly adjacent to Descemet’s membrane (compared with fewer hyphae in the superficial or mid-stroma) may suggest a tropism of fungal hyphae for stromal GAGs. It is not uncommon for fungal infections of the corneal stroma to progress to full thickness ulcers and culminate in corneal perforation.

DISEASE INCIDENCE

No breed, gender, or age predilection exists for fungal keratitis in horses. Geographic distribution is perhaps the most common risk factor for fungal keratitis in horses. Keratomycosis is more prevalent in horses that reside in humid climates than in arid climates. Disease occurrence may be seasonal in certain geographic regions of the country. Temperature and humidity may not favor fungal propagation except during certain times of the year. In subtropical environments such as the southeastern United States, the incidence is perpetual. In other parts of the country, higher incidence occurs during summer and fall months.

CLINICAL SIGNS

Fungal keratitis may be evident as ulcerative keratitis, stromal abscess, or corneal perforation with subsequent iris prolapse. Ulcerative keratitis is defined as loss of the corneal epithelium and its basement membrane and may be associated with or without loss of various amounts of corneal stroma. Ulcerative keratitis is classified by depth of

stromal involvement and can be superficial, midstromal, or deep. A corneal stromal abscess results from inoculation of the stroma with bacterial or fungal organisms with or without subsequent epithelial closure that seals the organism in the stroma. Iris prolapse refers to a full-thickness defect in the cornea or limbus with iris protrusion.

Blepharospasm (squinting), epiphora (tearing), photophobia, and miosis (constriction of the pupil) are the most common clinical signs in horses with fungal keratitis. Corneal edema may be present focally—surrounding the lesion—or diffusely—involving the entire cornea. Corneal neovascularization occurs slowly. Chemosis (conjunctival edema) may be evident and attributable to rubbing or to protease release. Fungal ulcers range from minor erosions or large intrastromal lesions with multiple punctate (“satellite”) lesions that surround the predominant lesion (Color Plate 11), as superficial plaquelike lesions with or without stromal loss (Color Plate 12), or as deep keratitis. Fungal ulcers may have a raised, roughened edge and may appear yellow-green or white in color. Corneal stromal abscesses appear as ivory- to yellow-colored infiltrates in the corneal stroma and may or may not have intact epithelium overlying the entire cornea. When a fungal ulcer progresses to perforation and iris prolapse, the protruding iris may appear brown if the anterior iris surface protrudes or black if the posterior surface of the iris protrudes. The anterior chamber is usually shallow compared with the normal fellow eye. Hypopyon (see Color Plate 12) or fibrin may be present in the anterior chamber with any of the three manifestations of fungal keratitis.

DIAGNOSIS

Differential diagnoses include bacterial keratitis, indolent ulcer, corneal degeneration, corneal dystrophy, equine herpesvirus keratitis, eosinophilic keratoconjunctivitis, and equine recurrent uveitis. Diagnosis of fungal keratitis is based on clinical signs and cytologic (Color Plate 13) or histopathologic (Color Plate 14) observation of fungal hyphae or by fungal culture. All three tests are valid and useful to determine whether fungi are present; however, growth of fungal organisms in culture does not definitively diagnose fungal keratitis, because fungal organisms are normal resident ocular flora.

Fungal culture and cytologic examination are performed routinely on all eyes with corneal ulceration presented to our hospital, and fungi are detected in approximately 85% of eyes with fungal infection at the University of Florida in Gainesville, Fla. Sedation and auriculopalpebral nerve block are performed to facilitate examination. Culture of the lesion should be performed before application of any topical medications. Breaking the seal of the transport media moistens the culturette swab. The tip of the culturette swab should then be rubbed gently across the lesion, ensuring not to touch the horse's eyelids or human fingers. Alternatively, a sterile, blunt instrument (Kimura platinum spatula) may be used to gently scrape the periphery of the lesion to collect the sample. Material collected is then transferred to the tip of the culturette swab, and the swab is inserted back into its sterile transport vial and submitted to the laboratory. Fungal cultures are plated on Sabouraud dextrose agar to enhance fungal

and yeast growth and mycobiologic agar to enhance fungal growth and inhibit bacterial growth. When fungal organisms are suspected, the best growth results are achieved when samples are collected from the cornea or conjunctiva with a sterile, blunt instrument and are inoculated *directly* onto fungal culture medium (Sabouraud's dextrose medium). Fungal susceptibility testing is available at certain laboratories, but *in vivo* and *in vitro* results are often very different. It may take days to weeks to obtain culture results because some fungi are slow-growing. Rapid diagnosis may be obtained by cytologic examination. Fluorescein sodium dye should be instilled topically on every eye suspected of having a corneal ulcer. Rose bengal dye should also be used and may help detect early fungal keratitis lesions. These topical dyes are usually applied after obtaining corneal tissue (scraping) for fungal culture.

Before collection of corneal scrapings for cytologic examination, topical anesthetic (0.5% proparacaine hydrochloride) is applied to the cornea. The handle end of a number 10-Bard Parker scalpel blade may be used to gently scrape the lesion to obtain material. The cellular material collected should be gently smeared or rolled on a slide and heat or ethanol-fixed before staining. Staining with new methylene blue, hematoxylin and eosin, or Gomori methenamine silver is recommended to evaluate for the presence or absence of fungal hyphae (see Color Plate 13). It is not possible to determine the genus or species of fungus present based on cytologic examination. Detecting fungal hyphae by histopathologic examination (see Color Plate 14) is useful for larger corneal sections that are removed with the corneal scraping technique or during surgical keratectomy and conjunctival graft placement.

TREATMENT

Treatment of fungal keratitis has been reported to have highly variable success rates. However, with intensive medical therapy and judicious use of surgical therapy, saving the eye and vision should be expected. The goals of treatment are to control the infection—both fungal and secondary bacterial—preserve vision, and control inflammation and pain. Placement of a subpalpebral lavage tube (see Chapter 9.3: “Ocular Therapy”) facilitates medical treatment of fungal keratitis because therapy is frequent and long-lasting.

Ulcerative fungal keratitis may be treated medically or with a combination of medical and surgical therapies. Concurrent treatment of the corneal infection and the resultant iridocyclitis must be undertaken. Clinical signs of iridocyclitis may become more severe once antifungal therapy is initiated and fungal hyphae begin to die. Most antifungal drugs are fungistatic and not fungicidal, and most do not penetrate the cornea well. Therefore prolonged therapy is usually necessary. Standard medications include topical administration of an antifungal drug (Table 9.7-1) applied 4 to 6 times daily and a topical administration of a mydriatic/cycloplegic drug (1% atropine) up to 4 times daily to maintain pupil dilation. Topical application of a broad-spectrum antibiotic drug is also recommended because concurrent bacterial infection occurs between 30% to 60% of the time in eyes with fungal keratitis. A systemic nonsteroidal antiinflammatory drug, such as flu-

Table 9.7-1
Antifungal Drugs

Drug	Drug Class	Treatment Protocol	Comment
natamycin 5% suspension (Natacyl 5% ophthalmic suspension)	Polyene antibiotic	Topically q4-6h	Limited corneal penetration; dilution to 3.33% for use with subpalpebral lavage system
amphotericin B (Fungizone)	Polyene antibiotic	0.15% solution in 5% glucose topically q4-6h daily	Better activity against yeast
miconazole (Monistat 7)	Imidazole	2% vaginal cream topically q4-6h daily	Not for use with subpalpebral lavage system; good corneal penetration; some irritation possible
miconazole	Imidazole	1% solution used topically q4-6h daily	Good for subpalpebral lavage system use; available from compounding pharmacies
itraconazole (Sporanox)	Synthetic triazole	3 mg/kg PO q12h	Not for use with subpalpebral lavage system; available from compounding pharmacies
itraconazole	Synthetic triazole	1% with 30% DMSO topically q4-6h times daily	
fluconazole (Diflucan)	Bistriazole derivative	4 mg/kg PO q24h	
ketoconazole (Nizoral)	Imidazole derivative	30 mg/kg PO q24h	
silver sulfadiazine 1% cream (Silvadene cream)	Antimicrobial	Topically q4-6h	Not for use with subpalpebral lavage system
povidone iodine 5% solution	Antiseptic	Topically q24h	Irritating to conjunctiva

PO, By mouth; q12h, every 12 hours; DMSO, dimethyl sulfoxide.

nixin meglumine or phenylbutazone, is used for its antiprostaglandin properties twice daily, and then the frequency is reduced as dictated by response to treatment.

Topical treatment with an anticollagenolytic substance is indicated when stromal melting is evident or anticipated. Autologous, sterile serum or plasma may be applied as frequently as possible. Acetylcysteine 10% or potassium EDTA 0.05% may also be used for their ability to inhibit protease activity.

Surgical treatment may be necessary in eyes that do not respond to appropriate medical therapy. This determination is made by resolution of iridocyclitis and clinical signs of ocular pain. The latter include dilation of the pupil, decreased squinting, presence of corneal vascularization, and healing of the ulcer. Eyes with fungal ulcers that have collagenase activity and are melting should be considered candidates for surgical treatment.

Corneal stromal abscesses may be treated similarly to ulcerative fungal keratitis. Superficial abscesses will often heal with prolonged topical medical therapy. Deep stromal abscesses are more likely to be caused by fungal organisms than by bacteria organisms and often respond better to surgical therapy such as penetrating keratoplasty

or posterior lamellar keratoplasty. Stromal abscesses that respond to medical therapy often require 6 to 8 weeks of treatment.

Iris prolapse that results from a ruptured deep fungal ulcer should always be considered for surgical intervention. Tectonic support in the form of donor corneal tissue as well as a conjunctival pedicle or bridge flap should be offered to the client. Enucleation is also a valid treatment alternative because the visual outcome for eyes with ruptured ulcers is worse than for traumatic lacerations.

Supplemental Readings

- Andrew SE, Brooks DE, Smith PJ et al: Equine ulcerative keratomycosis: visual outcome and ocular survival in 39 cases (1987-1996). *Equine Vet J* 1998; 30:109-116.
- Barton MH: Equine keratomycosis. *Comp Cont Educ Pract Vet* 1992; 14:936.
- Brooks DE: Equine ophthalmology. In Gelatt KN (ed): *Veterinary Ophthalmology*, 3rd edition, Philadelphia, Lippincott Williams & Wilkins, 1999.

CHAPTER 9.8

Ocular Squamous Cell Carcinoma and Sarcoid

ANNE J. GEMENSKY

WARREN L. BEARD

Columbus, Ohio

Squamous cell carcinoma (SCC) and sarcoid are the most commonly reported neoplasms in horses. The eye and periocular region are the most common locations for SCC, and the periocular region is the second most common location for sarcoid in horses. Both neoplasms may masquerade as other neoplastic or nonneoplastic ocular diseases. Sarcoid and SCC are locally aggressive neoplasms, but only SCC may metastasize. Early diagnosis and treatment may diminish the risk of recurrence and/or metastasis.

SQUAMOUS CELL CARCINOMA

Squamous cell carcinoma SCC is the most common ocular neoplasm that affects horses. Early recognition and treatment of the neoplasm is imperative because prognosis varies considerably depending on lesion location and extent of tissue involvement (Table 9.8-1).

Risk Factors

SCC most commonly affects older horses, with reported mean ages of 8 to 11 years. However, younger horses can be affected, particularly those of predisposed breeds. Horses with little pigmentation of the periocular skin, eyelids, and conjunctiva are at greater risk, especially those with white, gray, and palomino coloring—such as the Appaloosa, Paint, and Pinto. Draft breeds, despite having pigmented eyelid margins, are predisposed to develop SCC, usually of the third eyelid or corneoscleral limbus, and may be affected as young as 3 to 4 years of age. Stallions and mares appear to be less susceptible to SCC than geldings are.

Exposure to ultraviolet (UV) light is a significant risk factor for development of SCC. Greater incidence of SCC occurs at higher altitudes and is attributable to greater exposure to UV radiation. UV light may induce proliferation of keratinocytes (actinic keratosis) that subsequently infiltrate the epithelial basement membrane and populate the underlying dermal layer. Another proposed mechanism of UV light involvement is solar radiation-induced gene mutation within the cell nucleus. Solar radiation results in an increase in the rate of DNA replication and insufficient DNA repair mechanisms.

Squamous cell carcinoma may develop from a carcinoma *in situ*, where neoplastic proliferation of epithelial

cells occurs but remains confined within the epithelium by the basement membrane. Sites of previous injury appear to be susceptible, particularly if healing is delayed. Additionally, sites of chronic inflammation, infection, or keratosis (proliferation of keratinocytes) are at greater risk for metaplastic transformation to SCC. Keratosis may be induced by chronic inflammatory conditions such as allergic blepharitis or by exposure to exudates or irritating chemicals. Bovine papillomavirus has also been implicated in development of SCC in horses.

Clinical Signs

Squamous cell carcinoma has a predilection for mucocutaneous junctions. Ocular sites are most common and constitute up to 40% to 50% of reports. Next most common are the external genitalia and skin. The most common sites of ocular involvement are the corneoscleral junction (limbus), nictitating membrane, medial canthus and eyelids (Color Plates 15 through 20). SCC usually results in solitary masses, but adjacent sites and the prepuce are at risk for development of the neoplasm. Early, preneoplastic lesions may appear as hyperemic, roughened, or ulcerated lesions located on the eyelid margin, leading edge of the nictitating membrane, or bulbar conjunctiva at or near the limbus; the temporal limbus is most commonly reported. Limbal neoplasms may originate from the bulbar conjunctiva and may infiltrate the cornea. Limbal SCC is a friable, raised, vascularized mass and may have a cobblestone-like appearance. Blood vessels usually extend beyond the margins of the neoplasm into the clear cornea. Masses of the eyelid and nictitating membrane have a similar appearance. However, the proliferative form may be pedunculated with a very broad base, whereas the ulcerative form is typified clinically by erosion of the eyelid margins, medial canthus, and leading edge of the nictitating membrane. Both forms may be detected in the same location. A white, inspissated, foul-smelling exudate that contains a mixed bacterial population often occurs on the surface of all types of SCC masses.

Differential Diagnoses

Papilloma may appear similar to SCC, but it is nonneoplastic and noninvasive and usually has a narrow pedunculated base. Other diseases that have similar clinical appearances

Table 9.8-1
Prognosis Associated with Treatments for Ocular and Periocular Squamous Cell Carcinoma and Sarcoid

Disease	Prognosis	Surgery	Cryosurgery	Surface Radiation	Interstitial Radiation	Chemotherapy	Immunotherapy	Hyperthermia	CO ₂ Laser
SCC-limbus	Good	++	+/-	++	-	+/-	-	-	+
SCC-nictans	Fair-good	++	+	-	+	(topical) +	-	-	-
SCC-medial canthus	Guarded	+/-	+	-	+	+	-	+	+
SCC-eyelid	Guarded	+	+	+	+	+	-	+	+
SCC-orbit/sinus/lymph node	Poor	+/-	-	-	-	+/-	-	-	-
Sarcoid	Fair-good	+/-	+	-	+	+	+	+/-	+

SCC, Squamous cell carcinoma; ++, treatment of choice; +, viable treatment option; +/-, efficacious in some cases; -, not recommended or not possible.

include habronemiasis, eosinophilic conjunctivitis, foreign body granuloma, amelanotic melanoma, and myriad other causes of blepharitis or keratoconjunctivitis. Equine cutaneous mastocytoma also may affect the periocular tissue, but the mass is usually solitary and nonulcerated.

Diagnostic Methods

Squamous cell carcinoma is most commonly diagnosed by its classic clinical appearance. However, because SCC may masquerade as other neoplastic or nonneoplastic ocular diseases, histologic examination should be used to definitively confirm the tentative clinical diagnosis. Additional examination techniques are helpful to determine gross extent of involvement and prognosis as well as to establish a therapeutic plan. Palpation of the eyelids, globe, and orbital bone with a gloved finger inserted into the conjunctival fornix; assessment of facial symmetry; and palpation of the regional lymph nodes and parotid salivary gland should be done. If orbital bone is involved or if distortion of facial bone or lymphadenopathy is detected, fine-needle aspiration (FNA) and cytology, biopsy, skull radiography, and/or endoscopy of the nasal passages may be useful to determine whether local extension into bone and adjacent sinuses or metastasis has occurred. If a mass appears to be localized, surgical and/or medical treatment may be warranted without cytologic or histologic confirmation. However, excised tissues should always be submitted for histologic confirmation and evaluation of surgical margins.

Cytology obtained by scraping the surface of the mass or FNA may be suggestive of SCC. However, the cellular characteristics of SCC are similar to those observed with epithelial cell reaction to chronic inflammation or infection. Neoplastic and reactive keratinocytes both demonstrate a high nuclear-to-cytoplasmic ratio, variable cell and nuclear size, and multiple nucleoli. Excisional, wedge, or punch biopsies are useful for histologic evaluation of SCC (see Color Plate 19), and often these biopsies can be obtained in a standing, sedated horse.

Prognosis

The prognosis for SCC varies by location and extent and method of treatment (see Table 9.8-1). SCC tends to be slow to metastasize, and metastatic rates of 6% to 18% have been reported. Regional lymph nodes and salivary glands and occasionally the lungs are sites of metastasis. Local infiltration is more typical as cords of neoplastic cells extend into adjacent soft tissue or bony structures. The orbit, sinuses, and nasal cavity are most commonly affected by extension of ocular SCC.

Factors that affect survival time in horses are size, site, number, and recurrence of neoplasms. Prognosis is generally favorable for neoplasms less than 2 cm, for those that occur at the limbus, and for solitary, circumscribed neoplasms of the leading edge of the nictitating membrane. Prognosis worsens with increased size of the mass, chronicity, diffuse eyelid involvement, local infiltration of orbital and adnexal structures, and metastasis. Death in horses attributable to SCC is usually by euthanasia because of poor quality of life or financial constraints rather than

direct results of tumor infiltration or metastasis. In one report, SCC less than or equal to 2 cm had a median survival time of at least 9 years, whereas SCC of sufficient size or extent to invade the orbit had a median survival time of only 9 months. Recurrence substantially affected prognosis; one or more incidents of recurrence dramatically decreased survival time. Recurrence rates of 25% to 45% are reported for horses treated, and recurrence appears most likely when SCC affects the eyelid and nictitating membrane. Limbal SCC has the best prognosis for survival, with over one-half of affected horses still alive at 9 years and a 3.8 times greater chance of survival compared with horses with eyelid SCC, in which only 52% were alive at 38 months. Cure rates of 89% to 100% have been reported for limbal SCC—a higher rate than achieved for eyelid SCC. Reduced likelihood of metastasis and recurrence is likely attributable to confinement of SCC by the avascular corneal and scleral collagen and the ability to excise and administer adjunctive therapy at the limbus.

Treatment

Options for treatment include wide surgical excision with or without adjunctive therapy, intralesional chemotherapy, immunotherapy or radiation, and topically applied surface therapy, which can include chemotherapy, cryotherapy, β -radiation, and radiofrequency-induced hyperthermia. A detailed description of each type of treatment is beyond the scope of this chapter. Therefore discussion will focus on therapies considered by these authors to be most effective, readily available, and cost-effective.

Surgery and Adjunctive Treatment

Surgical excision with adjunctive topical or intralesional therapy is typically the best option for cure. A significantly higher recurrence rate is seen when surgical excision is used as the sole mode of therapy, except for cases of early and localized SCC involvement. Curative treatment of approximately 85% exists for well circumscribed SCC of the leading edge of the nictitating membrane that are treated by surgical excision alone when the full extent of the T-shaped cartilage is removed with the nictitating membrane. Recurrence of SCC at the base of the nictitating membrane is common when the initial surgical excision fails to remove all of the nictitating membrane. Incomplete excision also results in the most aggressive form of local infiltration reported because the ventral conjunctival fornix is not a readily visible location for early detection of SCC growth. For the life of the horse, clients should be advised to monitor the primary site for recurrence and also other sites predisposed to occurrence of a different SCC. Postoperative care includes application of broad-spectrum topical antimicrobial drug and oral administration of systemic nonsteroidal antiinflammatory drugs as needed for tissue swelling and discomfort. Nictitating membrane removal does not significantly affect ocular health or cosmetic appearance in horses.

Limbal SCC is readily cured by conjunctivectomy and keratectomy of the mass followed by surface β -irradiation. Strontium-90 (^{90}Sr) is applied using a handheld applicator at a recommended total surface dose of 200 to 250 Gray and extending at least 2 mm beyond the visible margins

of the mass. Minimal overlap should occur when multiple applications are used to treat a large mass. Treated eyes are typically comfortable during the postoperative period. Corneal ulceration commonly occurs after treatment but usually heals in 7 to 10 days. Ulcers associated with treatment should be treated topically with a broad-spectrum antibiotic every 6 hours, and atropine should be used as needed to dilate the pupil. Flunixin meglumine should also be administered orally or intravenously for 7 to 10 days. In conjunction with surgical cytoreduction of limbal SCC, ^{90}Sr provided 87% to 100% cure rates for up to 5 years of follow-up. ^{90}Sr may also be effective for early eyelid or conjunctival SCC if the mass is small and superficially located or is surgically debulked before treatment.

Larger and deeper eyelid masses require surgical debulking and adjunctive interstitial radiation or chemotherapy. Many blepharoplastic procedures have been described to repair postexcisional eyelid defects in horses. A modified H-plasty is performed most frequently, but excessive tension at the wound incisions often requires additional modifications such as releasing incisions. Enucleation is required when extensive tissue involvement prevents reconstruction of a functional eyelid. Because of the difficulty of surgical reconstruction, topical and intralesional chemotherapy and radiation are viable treatment alternatives.

Brachytherapy

Brachytherapy is a treatment modality in which radiation is delivered from a sealed source and is applied directly to the affected area. Brachytherapy is the most common form of radiation used to treat SCC, including surface therapy, as with a β -irradiation using a handheld probe (usually ^{90}Sr) and interstitial (intralesional) implantation of the radioactive source. Squamous epithelium and glandular tissue generally have intermediate susceptibility to radiation, and microscopic neoplastic nests of cells are susceptible to radiation therapy. Massive tumors in which less than 90% of the tumor can be excised are resistant and result in a poor prognosis. Surface therapy is beneficial because high doses of radiation can be delivered directly to the target tissue with a limited amount of exposure of adjacent normal tissue. Moreover, postoperative isolation of the horse is not required after β -irradiation and remission has been achieved in up to 90% of periocular neoplasms treated by β -irradiation. Specific licensing is required of the person who administers the radiation, and precautions must be taken to reduce human exposure.

A variety of radioactive isotopes have been used for interstitial treatment of SCC and include iridium-192, radon-222, gold-198, cesium-137, cobalt-60, and iodine-125 in seed-type or ribbon-type implantation devices. Interstitial therapy provides a continuous low dose of radiation over a short period of time and has resulted in 75% to 100% nonrecurrence rates for at least one year. However, availability of interstitial therapy is limited because of strict training and licensing requirements, approved handling facilities, patient isolation, and disposal protocols.

Intralesional Chemotherapy

Intralesional injection of cisplatin and 5-fluorouracil (5-FU) has been successful in treating periocular SCC. Cisplatin is

an alkylating agent that binds to DNA and inhibits replication, whereas 5-FU is an antimetabolite. Either cisplatin or 5-FU may be used, but both drugs should not be combined for intralesional injection. Drugs injected intralesionally are rapidly eliminated and do not maintain therapeutic levels at the tumor site unless a repositol formulation is prepared. Either drug may be mixed with filter-sterilized medical-grade sesame oil to create a suspension to prolong drug presence in the tissue. Additionally, sesame oil may have innate antineoplastic properties by inducing an antigenic effect in affected tissue.

Without surgical debulking before treatment, intralesional injection of cisplatin resulted in no recurrence for 2 years in 72% of horses with periocular SCC. Remission rates are improved when treatment of large tumors ($\geq 20 \text{ cm}^3$) is intensified with higher drug concentrations or combined with surgery. Although relatively expensive, the drug is readily available and can be administered in a standing horse. To do so, 10 mg of 3.3 mg/ml cisplatin powder is combined with 1 ml sterile water and 2 ml sesame oil and mixed by pumping the mixture between 2 syringes connected by a stopcock to compound the emulsion. Injections at a dose of 1 mg/cm^3 for tumors 10 to 20 cm^3 should be repeated every 2 weeks for 4 treatments. Cisplatin diffuses only 5 mm from the site of tissue injection; therefore injections must not exceed a distance of greater than 1 cm from each other. Multiple planes of injection may be required for large neoplasms to ensure saturation of the neoplastic tissue. Local tissue inflammation, swelling, and ulceration are expected transiently (7-10 days) but do not reduce healing rates of surgical wounds or preclude a cosmetic result after remission. Systemic toxicity or other serious side effects have not been reported. Bleomycin is equally effective against SCC when injected intralesionally but is substantially more expensive.

Although reports of response of SCC to intralesional 5-FU have not been favorable, complete remission resulted in several horses treated with 5-FU (see Color Plates 17 and 18) at The Ohio State University in Columbus, Ohio. 5-FU (50 mg/ml) is suspended in a 1:1 ratio with sesame oil and injected into the mass once weekly for 4 treatments. Topically, 5-FU 1% solution (q8h) or 5% cream (q24h) and mitomycin C (q6h) have shown some promise in treatment of superficial periocular carcinoma *in situ* and of genital SCC. Thickness of treated tissue cannot exceed 2 to 3 mm because these drugs penetrate tissues poorly. Topical 5-FU should not be used for nodular or invasive neoplasms, because the surface may appear tumor-free while neoplastic cells proliferate and infiltrate tissues and are undetected beneath the skin surface. Moreover, topical 5-FU has photosensitizing effects; therefore exposure to sunlight must be limited during treatment.

Cryotherapy

Cryotherapy is a readily available, inexpensive, and effective treatment for SCC with success rates of 66% to 87% for cutaneous SCC. Liquid nitrogen and nitrous oxide gas are both useful cryogens for treatment. Liquid nitrogen is used most commonly in horses and offers additional advantages because it is affordable, inert, nonflammable, nontoxic, and easy to use. However, nitrous oxide is easier to store for long periods of time. In an effort to limit exposure of normal

cornea to the cryogen, a plastic spatula should be placed over the cornea after a lubricant ointment is applied. Petroleum jelly may also be applied to periocular skin adjacent to the tumor to prevent accidental freezing. Use of a thermocouple is desirable to monitor temperature during treatment but may also be impractical (e.g., treatment of corneal SCC). If a temperature probe is not available to ensure a core temperature of at least -25°C , the surgeon should monitor the ice ball that extends from the cryoprobe. This ice ball should engulf the entire mass and extend 2 to 5 mm beyond the obvious margins. Runoff of liquid nitrogen must be controlled to prevent damage to normal tissues. Tissue necrosis, sloughing, fibrosis, and depigmentation may occur postoperatively.

It has been suggested that cryotherapy may result in a higher risk of recurrence than in other treatment modalities. This may be attributable to inability to adequately freeze the deep portion of large masses. Precautions such as surgical debulking before cryotherapy, use of at least two rapid freeze/slow thaw cycles, and implantation of temperature probes to ensure tissue temperatures of -20°C to -60°C may increase the likelihood of remission.

Additional Therapeutic Modalities

Carbon dioxide (CO_2) laser ablation and radiofrequency hyperthermia have also been used to treat superficial SCC in horses. Low-energy, defocused CO_2 laser treatment of limbal SCC resulted in flash boiling and vaporization of neoplastic cells at a controllable depth with minimal postoperative inflammation or discomfort but potentially delayed the rate of healing compared with surgical removal. Radiofrequency hyperthermia is useful only for masses that are superficial and less than 4 to 5 mm in diameter, because tissue penetration is limited. Hyperthermia may exacerbate the effects of radiotherapy or chemotherapy and improve nonrecurrence rates. Immunotherapy was effective in some large SCC in horses but is used more commonly to treat SCC in cattle and sarcoid in horses.

SARCOID

Sarcoid is a benign fibroblastic neoplasm of the skin and is the most common cutaneous neoplasm reported in horses, donkeys, and mules. A wide variety of clinical appearances and locally invasive behavior is typical of sarcoid; therefore a diagnostic and therapeutic challenge exists.

Risk Factors

Sarcoid most commonly affects young horses; onset of clinical signs has been reported between 3 and 7 years of age. American Quarter Horses and Thoroughbreds are at greater risk than are Standardbred horses, which appear to be more resistant. In donkeys, males are more likely to be affected than females are. Bovine papillomavirus (BPV) types 1 and 2 have been reported to cause equine sarcoid. Additionally, individual genetic predisposition is also evident. Immune status of the host may also be related. It has been postulated that a sarcoid susceptibility gene is linked to the major histocompatibility complex region to promote development of sarcoid in the presence of BPV. Exposure to flies may be a significant risk factor because flies

are thought to translocate sarcoid cells into open wounds of horses.

Clinical Signs

The clinical appearance of sarcoid differs substantially and has been described as occult, verrucous, or fibroblastic (Color Plates 21 through 24). Distinct entities are not always evident, and mixed forms also occur. The most common sites reported are the head, the ventral abdomen, and the limbs. Verrucous and fibroblastic forms or combinations of both are most commonly reported types that occur in the periocular region. The verrucous form is recognized as an area of alopecia, thickening, and hyperkeratosis with flaking and, in some cases, ulceration of the epidermal surface (see Color Plate 23). Verrucous sarcoid is occasionally mistaken for fungal dermatitis. The fibroblastic form appears as a firm, proliferative mass that may be covered with intact skin (see Color Plate 21) or may be ulcerated. Occult sarcoid is typified clinically as a black, alopecic plaque of thickened skin and is often undetected by an owner. Differential diagnoses include exuberant granulation tissue, granuloma, phycomycosis, cutaneous habronemiasis, dermatophilosis, papilloma, squamous cell carcinoma, and several other miscellaneous conditions. An experienced practitioner can usually make a clinical diagnosis by considering history, signalment, clinical appearance, and location of the lesion.

Diagnosis

Although sarcoid can usually be diagnosed based on clinical appearance, it may also have an unusual appearance, appear in an unusual location, or arise within a wound such that it is not immediately recognized. A punch or excisional biopsy may be used to obtain tissue for histologic evaluation and confirm a diagnosis in such instances. Fine-needle aspiration and cytology are not helpful because sarcoids do not exfoliate cells readily. Biopsy of a sarcoid should not be performed without the intention of subsequent and timely treatment because the remaining neoplastic cells may experience a rapid and invasive growth phase after surgical intervention. Biopsy occasionally results in tumor regression and may also be useful after treatment to differentiate granulation tissue from neoplasm regrowth, identify margins that may require subsequent resection, or confirm sites that require adjunctive treatment. Appropriate and early biopsy strategies allow more complete resections and fewer recurrences.

Treatment

Treatment options include surgical excision with wide margins, cryosurgery, immunotherapy, chemotherapy, and radiation therapy. None of the treatments are uniformly effective because of variable biologic behavior and response to treatment; some sarcoids are very aggressive and resistant to therapy, whereas others may regress spontaneously.

Surgical Excision

When removal of all neoplastic cells can be accomplished, it is the method of choice. Surgical excision as the sole



Color Plate 1 A scene as viewed by humans.



Color Plate 2 The same scene as in Color Plate 1 corrected for equine visual acuity and color perception.



Color Plate 3 A melting corneal ulcer (keratomalacia) resulting from infection with *Pseudomonas aeruginosa*.



Color Plate 4 Photomicrograph of a cytologic preparation from a corneal ulcer showing fungal hyphae.



Color Plate 5 Stromal abscess with iris prolapse.



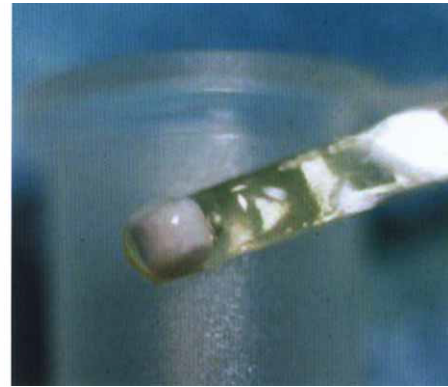
Color Plate 6 Clinical signs of acute equine recurrent uveitis (ERU). This horse has the "classic" form of ERU. An episode of acute uveitis, or flare-up, is evident with periocular swelling, epiphora, mucoid ocular discharge, blepharospasm, and corneal edema.



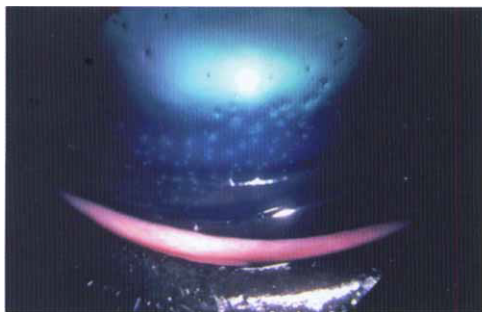
Color Plate 7 Clinical signs of acute recurrent uveitis (ERU). Photograph of an eye with typical signs of acute-onset ERU. Clinical signs include periocular swelling, hyperemic conjunctiva, diffuse corneal edema, hypopyon, and a miotic pupil.



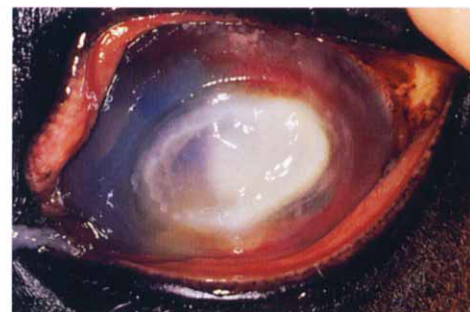
Color Plate 8 Clinical signs of chronic equine recurrent uveitis. Multiple recurrent episodes of uveitis have resulted in phthisis bulbi, atrophy of the corpora nigra, posterior synechia, and cataract formation.



Color Plate 9 Cyclosporine A intravitreal implant device.



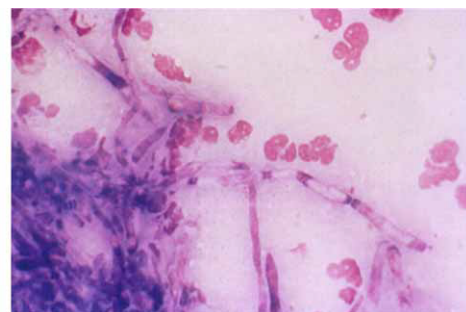
Color Plate 10 Retroillumination clearly demonstrates multiple small, superficial corneal opacities on the cornea of a horse. The opacities retained fluorescein sodium dye but were more obvious when viewed by retroillumination. These opacities typify the clinical appearance of equine herpesvirus 2 (EHV-2) keratitis. (Courtesy Dr. David T. Ramsey, East Lansing, Mich.)



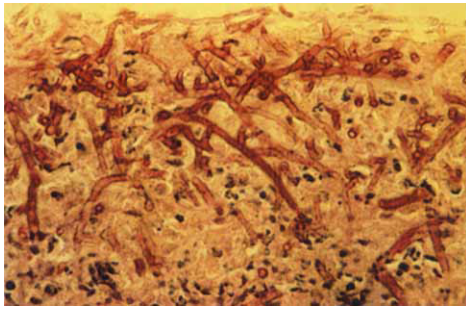
Color Plate 11 Photograph of the eye of a 20-year-old Arabian with a long-standing fungal ulcer. The ulcer has raised, roughened edges and appears yellow-green. Numerous "satellite" lesions (fungal microabscesses) are evident near the periphery of the ulcer. Prominent corneal vasculature is also evident, and the pupil cannot be seen.



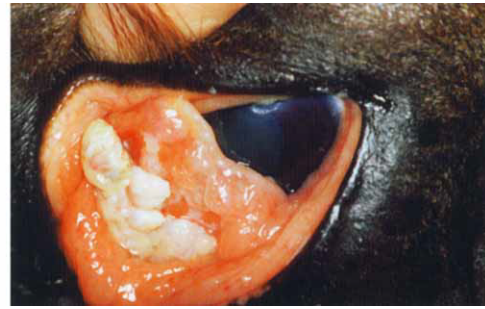
Color Plate 12 Photograph of the eye of a 6-year-old American Quarter Horse with a deep stromal abscess in the central, left cornea. Note the presence of hypopyon in the ventral anterior chamber, diffuse corneal edema, and superficial corneal neovascularization. Fluorescein sodium dye has been applied to the cornea, and there is no stain uptake.



Color Plate 13 Corneal cytology specimen obtained from a 2-year-old Thoroughbred horse with superficial fungal keratitis. The slide has been stained with Gomori methenamine silver, which causes the fungal hyphae to be seen as black elements.



Color Plate 14 A standing keratectomy specimen from a Thoroughbred yearling with a melting corneal ulcer. The sample is stained with hematoxylin and eosin, and multiple fungal hyphae can be seen in the superficial stroma.



Color Plate 15 Typical clinical appearance of squamous cell carcinoma (SCC) at this location. Proliferative mass of the nictitans with inspissated surface exudate.



Color Plate 16 Typical clinical appearance of squamous cell carcinoma (SCC) at this location. A SCC at the lateral limbus, infiltrating the cornea.



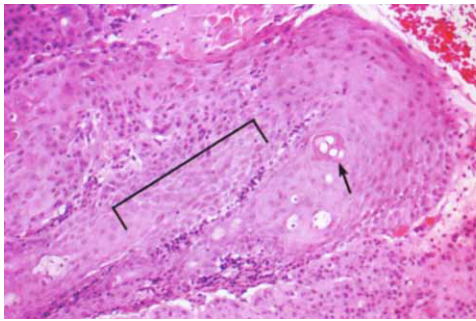
Color Plate 17 Typical clinical appearance of squamous cell carcinoma (SCC) at this location. Inflammation of a SCC of the lower eyelid near the medial canthus, 1 week after 5-fluorouracil (5-FU) injection.



Color Plate 18 Typical clinical appearance of squamous cell carcinoma (SCC) at this location. The same horse in Color Plate 17 1 year later. The mass near the medial canthus resolved after 5-fluorouracil (5-FU) injections; however, a new mass occurred in the middle of the lid 1 year later.



Color Plate 19 Syringe and stopcock method of suspending 5-fluorouracil (5-FU) in sesame oil before intratumoral injection. Sesame oil is filtered before mixing.



Color Plate 20 Photomicrograph depicting the histologic appearance of squamous cell carcinoma (SCC). Whorls of epithelial cells with multiple, prominent nucleoli surround central regions of keratin pearly (*arrow*). A region of prominent intracellular bridging is also apparent (*bar*). The image is an H&E stain, 42× magnification.



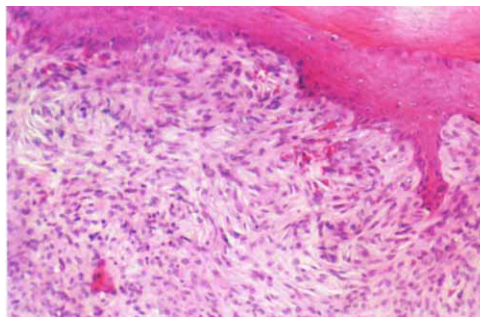
Color Plate 21 Typical clinical appearance of a multilobular fibroblastic periocular sarcoid in a 4-year-old American Quarter Horse. Notice the alopecia and hyperkeratosis.



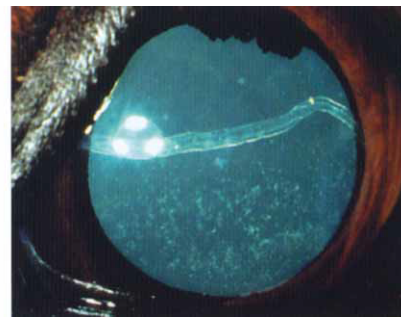
Color Plate 22 Complete regression and cosmetic healing are evident 3 months after completion of intralesional *Bacillus Calmette-Guérin* (BCG) treatment.



Color Plate 23 Typical clinical appearance of a verrucous sarcoid. The lesion is flat, thickened, and nodular.

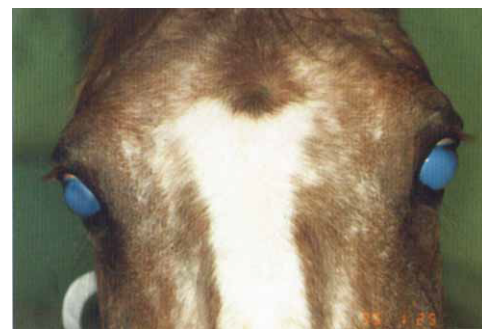


Color Plate 24 Photomicrograph depicting the histologic appearance of a sarcoid. Hyperkeratosis is evident at the top of the picture, with whorls of spindloid cells beneath the epidermis.



Color Plate 25 Linear opacities at the level of Descemet's membrane are often found in cases of early glaucoma in the horse.

Color Plate 26 Bilateral corneal edema and buphthalmos in a foal with congenital glaucoma. Intraocular pressures (IOP) were more than 80 mm Hg.



form of treatment is not usually successful because of the need to achieve wide surgical margins and lack of mobility of adjacent skin in the periocular area. When surgical treatment is used to excise all neoplastic tissue, function of the eyelids and remaining adnexal tissues is commonly destroyed. Therefore alternative treatment is recommended. Incomplete excision without ancillary treatment may lead to recurrence of highly aggressive sarcoid in up to 50% of horses. Enucleation or extensive blepharoplasty procedures may be required to facilitate complete tumor excision and close large periocular tissue defects. However, these techniques may be time-consuming and expensive. Additionally, not all sarcoids are amenable to surgical excision. Margins should be biopsied in advance to confirm the extent of the sarcoid, and all questionable areas should be removed with at least a 1 to 2 cm margin of normal tissue and submitted for histologic evaluation. If histologic evaluation suggests incomplete excision, immediate ancillary treatment with chemotherapy or cryosurgery should be considered.

Carbon dioxide laser ablation is advantageous compared with conventional scalpel excision in that excisional depth and area are precisely controlled and the surgical field is bloodless. In one study, an 81% success rate was reported for a 12-month follow-up period. To date, this is the only study that has directly compared the laser with conventional scalpel excision, and a conclusive benefit with respect to cure has not been reported.

Cryosurgery

Cryosurgery is very useful for small, new, or recurrent sarcoids and as an adjunct in the treatment of larger sarcoids after excision. Reported success rates for sarcoids treated by cryosurgery range from 60% to 100%. Cryosurgery appears to be most effective when it is combined with surgical debulking; it is inexpensive and fast and can be repeated if necessary. Details of the cryosurgery procedure are provided under the Treatment section of SCC in this chapter.

Immunotherapy

An immunologic basis for sarcoid regression has long been recognized. *Bacillus Calmette-Guérin* (BCG) cell wall extract and intact, killed, or live *Mycobacterium bovis* organisms are known to stimulate a nonspecific immune response that may result in regression of sarcoid. In these authors' experience, BCG is most useful to treat periocular sarcoids, probably because of extensive blood supply and resulting potential for immunogenic response in the periocular region. Success rates in various studies range from 34% to 100%, but in these authors' opinions, success approaches 75% for periocular sarcoids treated by intralesional injection of BCG.

Two forms of BCG are currently available—live (Thera Cys, Aventis Pasteur Inc., Swiftwater, Penn.) and cell wall extract (Regressin, Vetrepharm Research Inc., Athens, Ga.). The recommended dose is 0.2 ml injected intralesionally through a 25-gauge needle, repeated every 7 to 14 days for 3 or 4 treatments and injected at the same site each time. Manufacturer safety precautions should be followed to reconstitute the BCG product. Minimal soft tissue swelling

occurs with the first injection and is followed by a marked inflammatory reaction with subsequent injections. Necrosis and/or tumor regression may be evident beginning with the third injection. Treatment is discontinued if no response is seen after the fourth injection. Tumor regression may take place over several months. Fatal anaphylaxis is a possible adverse response to the injection; therefore pretreatment with flunixin meglumine (1.1 mg/kg) 30 minutes before tumor injection is advisable. All BCG protocols are empirical.

Interstitial Brachytherapy

Use of radiation therapy has been very successful to treat sarcoid in horses, even for sarcoids that were refractory to previous treatments. However, brachytherapy is not readily available in private practice. It is most useful to treat large sarcoids when surgical excision is not possible or when enucleation would otherwise be required to facilitate complete excision. Debulking the tumor decreases the amount of radiation required. Two commonly used isotopes are iridium-192 and gold-198. Reported success rates range from 87.5% to 100%. See the Treatment section under SCC for details of treatment.

Chemotherapy

Intralesional injection of cisplatin or 5-fluorouracil (5-FU) have demonstrated 70% to 90% success in treatment of sarcoids. Either drug may be placed into suspension with filter-sterilized sesame oil to prolong tissue drug levels after intralesional injection. Cisplatin is markedly more expensive than 5-FU but also may be more effective. See the Treatment section under SCC for details of treatment.

Prognosis

Although sarcoid in horses is not metastatic, it has a relatively high rate of local recurrence despite treatment, particularly when surgical excision was incomplete. Additionally, sarcoids in the periocular region may become quite large, thus compromising vision, ocular health, and cosmesis. Early application of appropriate diagnostic and therapeutic techniques may diminish the risk of tumor sequelae and recurrence (see Table 9.8-1).

Supplemental Readings

- Dugan SJ, Curtis CR, Roberts SM et al: Epidemiologic study of ocular/adnexal squamous cell carcinoma in horses. *J Am Vet Med Assoc* 1991; 198:251-256.
- Dugan SJ, Roberts SM, Curtis CR et al: Prognostic factors and survival of horses with ocular/adnexal squamous cell carcinoma: 147 cases (1978-1988). *J Am Vet Med Assoc* 1991; 198:298-303.
- Johnson PJ: Dermatologic tumors (excluding sarcoids). *Vet Clin North Am Equine Pract* 1998; 14:625-658.
- Rebhun WC: Tumors of the eye and ocular adnexal tissues. *Vet Clin North Am Equine Pract* 1998; 14:579-606.
- Theon AP: Intralesional and topical chemotherapy and immunotherapy. *Vet Clin North Am Equine Pract* 1998; 14:659-671.
- Theon AP: Radiation therapy in the horse. *Vet Clin North Am Equine Pract* 1998; 14(3):673-688.

CHAPTER 9.9

Equine Glaucomas

DENNIS E. BROOKS

Gainesville, Florida

Before a discussion of equine glaucomas begins, it is important to review some of the normal physiology that is involved in the maintenance of intraocular pressure and some of the reasons that glaucoma can have serious consequences in horses. Retinas of large eyes, as in the horse, have an extensive sensory surface area and vast numbers of photoreceptors and retinal ganglion cells (RGC) that have axons, which merge toward the optic papilla ventral to the posterior pole of the globe and form the optic nerve. Optic nerves of these large eyes have a large cross-sectional area and contain a greater number of RGC axons compared with retinas of smaller eyes. The horse optic nerve contains an enormous population of large diameter optic nerve axons. Large RGC cells have large diameter optic nerve axons, extensive overlapping retinal receptive fields, and provide rapid transfer of visual input for detection of moving objects, which is a distinct advantage for the horse. However, large-diameter axons also are most susceptible to damage from glaucoma, a probable disadvantage for the horse.

The normal equine scleral lamina cribrosa is complex. The sieve-like scleral lamina cribrosa groups the RGC axons into optic nerve axon bundles and supports the axons as they pass through the sclera and exit the globe as the orbital portion of the optic nerve. Axoplasmic flow of optic nerve axons is normally subjected to a substantial pressure gradient between the intraocular and intraorbital spaces at the lamina cribrosa. Laminar pores in the center of the optic nerve tend to have thicker interbundle connective tissue that may protect axons in this region from damage attributable to altered intraocular pressure (IOP). Elevated IOP such as occurs in glaucoma exacerbates this pressure gradient, and is associated with posterior displacement of the lamina cribrosa and disruption of axoplasmic flow within axons comprising the optic nerve.

AQUEOUS HUMOR AND INTRAOCULAR PRESSURE

Production of aqueous humor by the ciliary body epithelium requires energy and the enzyme carbonic anhydrase. Aqueous humor passes from the posterior chamber, through the pupil into the anterior chamber, and then egresses through the iridocorneal angle (conventional outflow pathway), or through the iris, ciliary body, and sclera (unconventional outflow pathway). Studies indicate a potentially extensive unconventional aqueous humor outflow pathway in the horse. The delicate balance between production and egression of aqueous humor results in the IOP. The IOP in the horse ranges from 7 to 37 mm Hg,

with the mean IOP 23.3 ± 6.9 mm Hg when measured with a Tonopen applanation tonometer (Mentor O & O, Santa Barbara, Calif.). Failure to use auriculopalpebral nerve blocks during tonometry may result in slight overestimates of IOP. Such a nerve block is frequently necessary in fractious horses. If sedation is required for the ocular examination, IOP can be substantially reduced as illustrated by a study in which xylazine (Rompun) decreased IOP by 23% to 27%.

ETIOLOGY AND RISK FACTORS FOR EQUINE GLAUCOMA

The glaucomas are a group of diseases resulting from alterations of aqueous humor dynamics that cause an elevation of IOP above a level that is compatible with normal function of the retinal ganglion cells and optic nerve. Horses with previous or concurrent iridocyclitis, aged horses, and Appaloosas are at increased risk for development of glaucoma. Glaucoma has also been reported in the Paso Fino, Quarter Horse, Tennessee Walking Horse, Thoroughbred, Arabian, Welsh pony, American Saddlebred, and warmbloods.

The presence of active or inactive iridocyclitis appears to be a major factor in the development of glaucoma in horses. Elevated IOP is clearly the primary risk factor for rapid progression of optic nerve damage and blindness in the horse. Iris and ciliary body neoplasms can obstruct aqueous humor outflow and result in secondary glaucoma. Congenital glaucoma is reported in foals and associated with developmental anomalies of the iridocorneal angle.

DIAGNOSIS AND CLINICAL SIGNS

The infrequent diagnosis of glaucoma in the horse may be attributable, in part, to limited availability of tonometers in equine practice but also to the fact that large diurnal fluctuations in IOP occur, even in eyes with chronic glaucoma; therefore elevated IOP may be difficult to document.

Diagnosis of glaucoma in horses is based on clinical signs specific to glaucoma and elevated IOP. Glaucoma in horses may not be easily recognized in the early stages of the disease because clinical signs are typically inconspicuous. Generally, a low index of suspicion of glaucoma exists in the early stages—pupils are often only slightly dilated, and overt signs of discomfort are uncommon. Afferent pupillary light reflex deficits, linear corneal striae (Color Plate 25), decreased vision, lens instability, mild iridocyclitis, and optic nerve atrophy/cupping may also be found

in eyes of horses with glaucoma. Corneal edema and vascularization, buphthalmos (absolute enlargement of the globe; Color Plate 26), blindness attributable to optic nerve atrophy, and signs of ocular pain may characterize chronic glaucoma in the horse. Ulcerative exposure keratitis may also develop secondary to buphthalmos.

The IOP in glaucomatous horses does not remain consistently elevated, and large diurnal fluctuations in IOP occur with time. Frequent IOP measurements during the day may be necessary to detect transient IOP spikes. Wide diurnal variation in IOP not only obscures the diagnosis of glaucoma but also complicates monitoring the response to treatment. The IOP will eventually decrease in buphthalmic globes as the ciliary body atrophies.

Glaucoma in the horse results in early peripheral retinal and optic nerve damage with progression to generalized retinal and optic nerve atrophy. The horse eye frequently is able to tolerate elevations in IOP that would rapidly blind a dog; however, blindness is ultimately the end result. The marked number of axons in the optic nerve of the horse may act as an anatomic axonal reservoir that provides early protection against total loss of vision despite very high IOP. Large-diameter axons in the optic nerve are affected more rapidly and often than medium- to small-sized axons in horses with glaucoma. Although large retinal ganglion cells are involved with motion detection, stereopsis, and sensitivity to dim light, the effect of loss of large retinal ganglion cell axons on functional vision in the horse with early glaucoma is not known.

TREATMENT

The events and mechanisms that lead to obstruction of aqueous humor outflow and increased IOP in the horse are not completely known; therefore it is very difficult to initiate effective treatment. Medical management of equine glaucoma parallels the same general guidelines as that of other species, with the aims of treatment being to decrease the production and increase the outflow/egression of aqueous humor. The response to medical treatment is usually poor, and long-term prognosis for maintaining vision is guarded. Partial vision may be preserved for extended periods, despite dramatically high IOP that occurs in some glaucomatous horses. Various combinations of drugs and surgery may be necessary to reduce the IOP to a level that is compatible with preservation of functional vision in horses with glaucoma. Control of IOP can improve vision in horses with decreased vision caused by resolution of marked corneal edema and improvement of vascular perfusion. Glaucoma is particularly aggressive and difficult to control in the Appaloosa.

Medications that reduce aqueous humor production, such as topically administered carbonic anhydrase inhibitors and β -adrenergic antagonists, appear to be the most effective at lowering IOP in the horse (Table 9.9-1). Topically administered carbonic anhydrase inhibitor dorzolamide (Trusopt; 2% q8h) and orally administered carbonic anhydrase inhibitors acetazolamide (Acetazolamide; 1-3 mg/kg q6h PO) are useful. The topical miotic drugs demecarium bromide (Humorsol 0.25%; 0.12%-0.25% q12h), pilocarpine (Piloptic 2%; q6h), and the topical β blocker timolol maleate (Timoptic 0.5%; q12h)

Table 9.9-1
Topically Applied Medications
for Equine Glaucoma

Drug	Frequency of Application
0.5% timolol maleate (Timoptic 0.5%)	q12h
0.25% demecarium bromide (Humorsol 0.25%)	q12h
2-4% pilocarpine HCl (Piloptic 2%)	q6-12h
2% dorzolamide (Trusopt)	q12h

q12h, Every 12 hours; *q6-12h*, every 6 to 12 hours.

have been used to lower IOP in horses with varying degrees of success. Contemporary prostaglandin derivative drugs manufactured for ocular use (0.03% latanoprost) cause low-grade iridocyclitis and may exacerbate the IOP in horses with glaucoma. Conventional glaucoma treatment with miotics may provide varying levels of IOP reduction in horses; however, miotics and synthetic prostaglandins may exacerbate the clinical signs of iridocyclitis and should be used with caution in horses with mild or quiescent anterior uveitis.

Topical atropine (Atropine sulfate 1%) therapy was previously reported to reduce the incidence of glaucoma in horses with anterior uveitis. However, atropine does not appear to have the benefit of lowering IOP as once proposed and therefore should be used cautiously in horses with glaucoma because it may cause high spikes in IOP.

Antiinflammatory therapy, which consists of topically and systemically administered corticosteroid drugs and/or topically (flurbiprofen) and systemically (phenylbutazone [Phenylbutazone], flunixin meglumine [Banamine]) administered nonsteroidal antiinflammatory drugs also appear to be beneficial in the control of IOP.

Various surgical procedures have been used to control IOP and preserve vision in horses with glaucoma. In the glaucomatous horse with functional vision, the surgical options include transscleral laser cyclophotoablation, cyclocryoablation, and filtration gonioimplant procedures. When medical therapy is inadequate, neodymium: yttrium-aluminum-garnet (Nd:YAG) laser cyclophotoablation may be a viable alternative for long-term IOP control. Nd:YAG laser cyclophotoablation is very effective at controlling IOP and maintaining vision in the horse. This author recommends contact Nd:YAG laser cyclophotoablation application of 60 laser sites placed 5 mm posterior to the limbus and a power setting of 11 watts for 0.4 seconds duration per site for the glaucomatous equine eye. Clinical evidence indicates that laser cyclophotoablation is extremely efficacious at lowering IOP and maintaining vision in glaucomatous eyes of horses.

Filtration gonioimplant surgery to increase outflow of aqueous humor is experimental in the horse but has been successful. Glaucomatous eyes that are chronically

painful, blind, and buphthalmic should be enucleated or have an evisceration and intraocular prosthesis implanted.

Supplemental Readings

- Brooks DE: Equine Ophthalmology. In Gelatt KN (ed): Veterinary Ophthalmology, 3rd edition, pp 1053-1116, Baltimore, Lippincott Williams & Wilkins, 1999.
- Miller TR, Brooks DE, Gelatt KN et al: Equine glaucoma: clinical findings and response to treatment in 14 horses. *Vet Comp Ophthalmol* 1995; 5:170-182.
- Smith PJ, Samuelson DA, Brooks DE et al: Unconventional aqueous humor outflow of microspheres perfused into the equine eye. *Am J Vet Res* 1986; 47:2445-2453.

- Van der Woerd A, Gilger BC, Wilkie DA et al: Effect of auriculo-palpebral nerve block and intravenous administration of xylazine on intraocular pressure and corneal thickness in horses. *Am J Vet Res* 1995; 56:155-158.
- Van der Woerd A, Gilger BC, Wilkie DA et al: Normal variation in and effect of 2% pilocarpine on intraocular pressure and pupil size in female horses. *Am J Vet Res* 1998; 59:1459-1462.
- Wilcock BP, Brooks DE, Latimer CA: Glaucoma in horses. *Vet Pathol* 1991; 28:74-78.
- Willis AM, Robbin TE, Hoshaw-Woodard S et al: Effect of topical administration of 2% dorzolamide hydrochloride or 2% dorzolamide-0.5% timolol maleate on intraocular pressure in clinically normal horses. *Am J Vet Res* 2001; 62:709-723.

CHAPTER 9.10

Abnormal Ocular Discharge

DAVID T. RAMSEY
East Lansing, Michigan

Presence of an abnormal ocular discharge is a common reason for presentation of a horse for veterinary evaluation. An ocular discharge may be abnormal based on its volume or composition. Ocular discharge is most frequently classified based on its character—which can be serous, mucoid, mucopurulent, purulent, sanguineous—on whether it is chronic or acute, or on whether the discharge was acquired or was present since (or near) birth. When an ocular discharge is evident, a thorough ocular examination is indicated. A logical and methodical process should be used to determine the underlying cause of the discharge. When the ocular discharge is characterized as serous, particular consideration should be given to establish whether excessive lacrimation or epiphora is present. A brief review of the anatomy of the lacrimal system is required to understand abnormalities that result in ocular discharge.

FUNCTIONAL ANATOMY

Production of Tear Film

The tear film is a composite trilaminar structure that comprises a superficial lipid layer, a middle aqueous layer, and an inner mucous layer. The most superficial layer of the tear film is produced by the meibomian glands, which are located in the tarsal plate of the eyelid. The lipid layer impedes evaporation of the aqueous layer of the tear film that lies beneath it. The middle aqueous layer is produced primarily by the orbital lacrimal gland and the seromucoid gland of the nictitating membrane. A minor part of the aqueous layer of the tear film is also derived from

aqueous humor and serum. Both hydrostatic pressure exerted by aqueous humor in the anterior chamber and the osmotic gradient that exists across the cornea between the aqueous humor and tears because of tear evaporation favor a continuous flow of water from the aqueous humor side of the cornea into the tear film on the external corneal surface. Similarly, an osmotic gradient exists between tears and serum within the conjunctival vasculature that favors transmural movement of fluid from conjunctival vasculature into the tear film. The aqueous portion of the tear film contains protective (antibacterial) proteins, immunoglobulins (IgA), electrolytes, and oxygen. The inner (mucous) layer of the tear film is produced by the conjunctival goblet cells. The mucous layer coats the superficial corneal epithelial cells, increases the surface area, and binds the aqueous layer of the tear film to the epithelial cells. The tear film also contains a population of resident and transient microbial flora composed primarily of gram-positive bacteria and fungal organisms that, under appropriate circumstances, become opportunistic pathogens. Some of these same organisms are also responsible, in part, for maintenance of normal surface ocular health by producing substances (e.g., polypeptide antibiotics) that have antibacterial and antifungal properties that moderate the growth of opportunistic pathogenic organisms and transient flora. Although the trilaminar tear film provides a physical barrier to contact between bacteria and cells of the ocular surface, the constant movement of tears also serves to prevent microbial adherence and remove potentially infectious microbes and toxins. Tears also participate in the defense of the ocular surface by contributing nonspecific inhibitors of bac-

painful, blind, and buphthalmic should be enucleated or have an evisceration and intraocular prosthesis implanted.

Supplemental Readings

- Brooks DE: Equine Ophthalmology. In Gelatt KN (ed): Veterinary Ophthalmology, 3rd edition, pp 1053-1116, Baltimore, Lippincott Williams & Wilkins, 1999.
- Miller TR, Brooks DE, Gelatt KN et al: Equine glaucoma: clinical findings and response to treatment in 14 horses. *Vet Comp Ophthalmol* 1995; 5:170-182.
- Smith PJ, Samuelson DA, Brooks DE et al: Unconventional aqueous humor outflow of microspheres perfused into the equine eye. *Am J Vet Res* 1986; 47:2445-2453.

- Van der Woerd A, Gilger BC, Wilkie DA et al: Effect of auriculo-palpebral nerve block and intravenous administration of xylazine on intraocular pressure and corneal thickness in horses. *Am J Vet Res* 1995; 56:155-158.
- Van der Woerd A, Gilger BC, Wilkie DA et al: Normal variation in and effect of 2% pilocarpine on intraocular pressure and pupil size in female horses. *Am J Vet Res* 1998; 59:1459-1462.
- Wilcock BP, Brooks DE, Latimer CA: Glaucoma in horses. *Vet Pathol* 1991; 28:74-78.
- Willis AM, Robbin TE, Hoshaw-Woodard S et al: Effect of topical administration of 2% dorzolamide hydrochloride or 2% dorzolamide-0.5% timolol maleate on intraocular pressure in clinically normal horses. *Am J Vet Res* 2001; 62:709-723.

CHAPTER 9.10

Abnormal Ocular Discharge

DAVID T. RAMSEY
East Lansing, Michigan

Presence of an abnormal ocular discharge is a common reason for presentation of a horse for veterinary evaluation. An ocular discharge may be abnormal based on its volume or composition. Ocular discharge is most frequently classified based on its character—which can be serous, mucoid, mucopurulent, purulent, sanguineous—on whether it is chronic or acute, or on whether the discharge was acquired or was present since (or near) birth. When an ocular discharge is evident, a thorough ocular examination is indicated. A logical and methodical process should be used to determine the underlying cause of the discharge. When the ocular discharge is characterized as serous, particular consideration should be given to establish whether excessive lacrimation or epiphora is present. A brief review of the anatomy of the lacrimal system is required to understand abnormalities that result in ocular discharge.

FUNCTIONAL ANATOMY

Production of Tear Film

The tear film is a composite trilaminar structure that comprises a superficial lipid layer, a middle aqueous layer, and an inner mucous layer. The most superficial layer of the tear film is produced by the meibomian glands, which are located in the tarsal plate of the eyelid. The lipid layer impedes evaporation of the aqueous layer of the tear film that lies beneath it. The middle aqueous layer is produced primarily by the orbital lacrimal gland and the seromucoid gland of the nictitating membrane. A minor part of the aqueous layer of the tear film is also derived from

aqueous humor and serum. Both hydrostatic pressure exerted by aqueous humor in the anterior chamber and the osmotic gradient that exists across the cornea between the aqueous humor and tears because of tear evaporation favor a continuous flow of water from the aqueous humor side of the cornea into the tear film on the external corneal surface. Similarly, an osmotic gradient exists between tears and serum within the conjunctival vasculature that favors transmural movement of fluid from conjunctival vasculature into the tear film. The aqueous portion of the tear film contains protective (antibacterial) proteins, immunoglobulins (IgA), electrolytes, and oxygen. The inner (mucous) layer of the tear film is produced by the conjunctival goblet cells. The mucous layer coats the superficial corneal epithelial cells, increases the surface area, and binds the aqueous layer of the tear film to the epithelial cells. The tear film also contains a population of resident and transient microbial flora composed primarily of gram-positive bacteria and fungal organisms that, under appropriate circumstances, become opportunistic pathogens. Some of these same organisms are also responsible, in part, for maintenance of normal surface ocular health by producing substances (e.g., polypeptide antibiotics) that have antibacterial and antifungal properties that moderate the growth of opportunistic pathogenic organisms and transient flora. Although the trilaminar tear film provides a physical barrier to contact between bacteria and cells of the ocular surface, the constant movement of tears also serves to prevent microbial adherence and remove potentially infectious microbes and toxins. Tears also participate in the defense of the ocular surface by contributing nonspecific inhibitors of bac-

terial growth (lysosyme, lactoferrin, β -lysin, and immunoglobulins). In summary, this composite tear film structure provides a smooth optical surface for the cornea and lubricates, hydrates, nourishes, and removes waste products from the ocular surface.

Distribution of Tear Film

Movement of the eyelids, nictitating membrane, and globe functionally distributes the precorneal tear film meniscus across the ocular surface. Blinking propels tears toward the medial canthus and the medial, lower conjunctival fornix. The upper eyelid has far more active excursion movement during a blink compared with the lower eyelid, and is therefore of greater importance for distribution of the tear film in the horse. The nictitating membrane plays a negligible role in distribution of the tear film in the horse. Gravitational forces on the tear film result in collection of the largest volume of tears at the appositional interface between the lower lid and cornea. Apposition of the lower lid with the cornea prevents the normal volume of tears from spilling onto the face.

Elimination of Tear Film

Tears are eliminated from the ocular surface primarily by drainage through the nasolacrimal system but also by evaporation from the ocular surface. Factors that influence elimination of tears from the ocular surface include volume and compositional characteristics of the tear film, eyelid carriage and conformation, lid apposition against the cornea, anatomic and physiologic patency of the nasolacrimal system, and environmental humidity and temperature. Blinking favors drainage of tears by mechanically propelling tears toward the upper and lower lacrimal puncta located near the medial canthus. The lacrimal puncta are 2 to 3 mm in diameter, oval or slitlike openings that are oriented parallel with the lid margin. The puncta are located in the palpebral conjunctiva near the eyelid margin medial to the meibomian gland openings. The upper punctum is located approximately 8 to 9 mm from the medial canthus and the lower punctum located 5 mm from the medial canthus. Tears drain through the puncta into the upper and lower canaliculi, which are located beneath the palpebral conjunctiva and oriented parallel to the eyelid margin. The canaliculi converge and unify to form the lacrimal sac, a slightly dilated, conical lumen located in the lacrimal fossa—a shallow depression in the orbital surface of the lacrimal bone. The lacrimal sac passes through the lacrimal bone and is designated as the termination of the canaliculi and the origin of the nasolacrimal duct. The nasolacrimal duct is composed of intraosseous and membranous portions. The intraosseous portion of the nasolacrimal duct is enclosed in a bony canal that passes through the lacrimal bone and subsequently the bony lamina of the medial (nasal) wall of the maxilla. This portion of the nasolacrimal duct lies dorsal to an imaginary line that extends from the medial canthus to the infraorbital foramen and may be damaged if trephination—for example, by maxillary sinusotomy to access dental structures—occurs dorsal to this imaginary line. The intraosseous portion of the nasolacrimal duct is

continuous with the membranous portion of the nasolacrimal duct as it exits the maxilla and enters the lateral aspect of the middle meatus. The nasolacrimal duct then slopes ventrally as it enters the basal fold of the ventral nasal concha and is covered by a flat plate of cartilage that arises from the alar fold. The membranous portion of the nasolacrimal duct then exits the basal fold and bends laterally over the nasal process of the incisive bone before it ends in the nasal vestibule. The nasolacrimal duct terminates at the nasal punctum, a 2- to 5-mm in diameter, round, oval, or slitlike opening located just inside the nostril near the mucocutaneous junction on the ventromedial aspect of the nasal vestibule. The length of the nasolacrimal duct varies between 22 cm (ponies) and 40 cm (draft breeds). The diameter of the nasolacrimal duct lumen varies between 4 and 25 mm. The narrowest segment occurs as it passes through the lacrimal bone and maxilla. Several wide segments and focal dilations exist in the membranous portion. Patent accessory ducts extend from the membranous portion of the nasolacrimal duct and may open into the nasal cavity. Small blind sacculations also extend from the lumen of the nasolacrimal duct and can make catheterization of the distal duct lumen difficult.

CHARACTERIZING OCULAR DISCHARGE

Ocular discharge may be observed when any component of the tear film is overproduced or underproduced, when distribution of the tear film is ineffectual, or when partial or complete anatomic or physiologic obstruction to drainage of the tear film occurs. Ocular discharge may be composed of normal components of the tear film that are present in excess or deficient volume (serous and mucoid ocular discharge) or may contain inflammatory cells, exudate, or microbial organisms in concert with an ocular inflammatory response or infection. Whenever an ocular discharge is present, ocular and periocular tissues should be examined carefully to determine whether they appear clinically normal or abnormal (see Chapter 9.1: "Examination of the Eye").

Serous Ocular Discharge

Excessive Lacrimation versus Epiphora

When a serous ocular discharge is present, a distinction should be made between excessive lacrimation and epiphora as a cause of the discharge; however, making such a distinction is often problematic. Excessive lacrimation and epiphora often have the same clinical sign of spilling of tears from the palpebral fissure onto the face; however, the pathogenic mechanisms that result in lacrimation and epiphora differ substantially. Excessive lacrimation is defined as overproduction and discharge of tears with or without spilling of tears onto the face. Epiphora is defined as spilling of tears onto the face as a specific result of insufficient drainage of tears attributable to partial or complete nasolacrimal obstruction. Epiphora is not an absolute diagnosis; it is a clinical sign of obstruction of tear drainage and not a result of overproduction of tears. A serous ocular discharge attributable to excessive lacrimation or epiphora may be

exacerbated by exposure to environmental factors such as airborne particulate matter (dusts, pollens, molds), wind, and cold.

When excessive lacrimation is present, determining whether ocular pain accompanies the ocular discharge is important. Noxious stimuli, pain, or irritation of the eye, periocular tissues, and rostral nasal passages results in excessive tearing (reflex lacrimation) and subsequently serous ocular discharge. Common causes of surface ocular irritation or pain include abnormalities of the eyelashes (trichiasis, distichiasis) or eyelids (entropion in foals, ectropion associated with facial nerve paralysis in adult horses), ulcerative or nonulcerative keratitis, conjunctivitis, corneal or conjunctival abrasion and foreign bodies, ocular trauma, and topical exposure to irritating or toxic substances. Excessive lacrimation and concurrent signs of ocular pain (blepharospasm, ptosis, miosis, conjunctival and episcleral hyperemia, photophobia) are also often associated with iridocyclitis, glaucoma, and inflammatory orbital disease.

Presence of a serous ocular discharge—when ocular tissues appear clinically normal and when clinical signs of ocular pain are absent—substantially narrows the list of differential considerations for the ocular abnormality. Mild ocular surface irritation attributable to entrapment of hay, dust, or other debris in the conjunctival fornix and allergic conjunctivitis are considerations for excessive lacrimation and clinically normal-appearing ocular tissues without clinical signs of ocular pain. Commonly, horses with a serous ocular discharge are examined, and the cause is not readily evident. When the structure and function of the eyelids appear normal and apposition of the eyelid margin against the cornea is normal, abnormal elimination/drainage of the tear film should then be considered.

Excluding entropion, which may functionally misdirect or impede the outflow of tears, the most common cause of a serous to seromucoid ocular discharge in a foal is congenital obstruction of the nasolacrimal duct. Epiphora in foals with congenital obstruction is typically mild until the foal is 3 to 4 months of age, which may be attributable to lower tear production in foals. Epiphora is invariably attributable to congenital atresia or dysgenesis of the distal (rostral) portion of the nasolacrimal system (atresia of the nasal meatus punctum/imperforate nasal punctum, dysgenesis of the distal portion of the nasolacrimal duct). Abnormalities of the proximal (caudal) nasolacrimal system (atresia of the lacrimal [eyelid] punctum, ectopic lacrimal punctum) have been reported infrequently. Close examination reveals absence of the nasal punctum and occasionally a fluctuant swelling in the nasal vestibule that represents a dilated membranous portion of the nasolacrimal duct. With chronicity, pooling of stagnant tears in the nasolacrimal duct favors bacterial overgrowth and subsequently development of a mucopurulent to purulent ocular discharge.

In adult horses, acquired obstruction of the nasolacrimal duct is common and may be attributable to intramural or extramural obstruction. Intramural obstruction is most common and is usually attributable to chronic bacterial or fungal dacryocystitis, foreign bodies, lacrimal calculi/dacryoliths, and parasites (habronemiasis, thelaziasis). Primary neoplasia of the nasolacrimal duct has not been described in the horse. Extramural obstruc-

tion may result in compression or appositional closure of the membranous or intraosseous portion of the nasolacrimal duct. Extramural obstruction may result from facial trauma in the area of the duct (fractures of the maxilla or lacrimal bone, maxillary sinusotomy), sinusitis, rhinitis, abnormalities of the maxillary dental arcade/periodontitis, bony callous formation, osteomyelitis, or neoplasia. Laceration of the eyelid or puncta or transverse laceration of the canaliculus may result in stenosis of the proximal nasolacrimal system. Immediate referral for surgical repair should be considered. Obstruction of the proximal nasolacrimal outflow pathways (punctum, canaliculus), although uncommon, typically results in a serous to mild seromucoid ocular discharge; mucopurulent ocular discharge occurs infrequently with obstruction of the puncta or canaliculi.

Mucoid Ocular Discharge

When the viscosity of the surface ocular secretions exceeds that which will readily egress through the nasolacrimal system, discharge of ocular secretions from the palpebral fissure onto the face may occur. Serous ocular discharge (suggestive of a nonseptic abnormality) typically develops into a mucoid discharge early in the clinical course of epiphora as a result of secondary dacryocystitis. Signs of ocular pain are absent, but chronic reflux of exudate emanates from the lacrimal puncta and palpebral fissure. Obstructions distal (rostral) to the lacrimal sac, if left untreated, favor bacterial growth within ocular secretions and the discharge associated with dacryocystitis assumes a mucopurulent to purulent character (see the following discussion).

An infrequent cause of a mucoid to mucopurulent ocular discharge in the horse is keratoconjunctivitis sicca (KCS). Although KCS has a low occurrence rate in the horse, the most common cause is secondary to traumatic disruption of parasympathetic nerve supply to the lacrimal gland. Parasympathetic fibers to the lacrimal gland course with the facial nerve, which passes through the region of the guttural pouch and stylohyoid bone, an anatomic area susceptible to trauma. Other causes of KCS in horses include exposure to plant toxins (Locoweed) and chemicals and aberrant migration or parasites into lacrimal gland tissue.

Mucopurulent and Purulent Ocular Discharge

A mucopurulent to purulent ocular discharge rapidly develops when pooling of stagnant tears favors bacterial overgrowth in the nasolacrimal duct. Obstruction to outflow of tears from the lacrimal sac or more distally in the nasolacrimal duct typically causes a mucopurulent to purulent ocular discharge. Bacterial dacryocystitis subsequently develops and often results in secondary conjunctivitis. Signs of ocular pain are absent, but chronic reflux of mucopurulent exudate emanates from the lacrimal puncta and palpebral fissure. When the nasolacrimal system is patent, irrigation of the nasolacrimal duct from the nasal punctum produces abundant, tenacious mucopurulent exudate that emanates from the lacrimal punctum and palpebral fissure. A mucopurulent ocular discharge is also typical in horses kept in a dusty environment and in horses with chronic allergic conjunctivitis. The mucopu-

ruent ocular discharge associated with chronic KCS is substantially less in volume and of greater viscosity. Additionally, clinical signs of ocular pain or discomfort are common in horses with KCS and are generally absent in horses with dacryocystitis.

Hemorrhagic Discharge

A serosanguineous or hemorrhagic discharge coming from the nasal punctum in the nasal vestibule may be misdiagnosed as epistaxis. Ulceration of the nasolacrimal mucosa may result from chronic sepsis (bacterial dacryocystitis), presence of an intraluminal foreign body, trauma (including repeated attempts to catheterize the nasolacrimal duct), vasculitis, and neoplasia.

DIAGNOSTIC CONSIDERATIONS

Measurement of Tear Production

Tear production is measured infrequently in horses and is only recommended when clinical signs suggest low tear production (mucoid to mucopurulent ocular discharge, ocular pain, dry, lackluster cornea with or without ulceration or abrasion, vascularization of the cornea). Commercially available Schirmer tear test strips are not manufactured for use in the horse but may be used to measure tear production (see Chapter 9.1: "Examination of the Eye").

Evaluation of Tear Distribution

Ineffectual tear distribution may occur with defects in the upper eyelid margin; rarely will a defect in the nictitating membrane (or its absence) result in abnormal tear distribution in the horse. Even sizable defects of the lower eyelid margin (focal absence associated with previous trauma) rarely result in abnormal tear distribution. When trichiasis is associated with a defect of the upper eyelid margin, excessive lacrimation may occur from surface irritation and ineffectual distribution of tears. Facial nerve damage that results in lagophthalmos may result in inadequate distribution. Topical instillation of fluorescein sodium dye may be used to evaluate distribution of the tear film.

Evaluation of Lacrimal Drainage

When excessive lacrimation has been eliminated as the reason for a serous ocular discharge, the upper and lower lacrimal puncta and nasal punctum should be evaluated to determine their presence, position, patency, and whether they appear moist or have abnormal (volume or character of) discharge. The nasal punctum in the nasal vestibule will appear dry when complete obstruction of the nasolacrimal system is present. Physiologic patency of lacrimal drainage may be evaluated with topical fluorescein sodium dye by the fluorescein pass test (Jones test). Fluorescein dye solution is instilled topically on the ocular surface and observed as it passes through the nasal punctum in the nasal vestibule. In most horses, passage occurs within one minute, but up to 5 minutes should be permitted. If passage of fluorescein is not observed, anatomic patency may be evaluated by use of a nasolacrimal cannula

attached to a syringe filled with irrigating solution (saline solution). Topical anesthetic solution is instilled 5 minutes before cannulation. Sedation may also be required. A 5 French (Fr) urinary catheter is inserted gently into the nasal punctum and advanced several centimeters (retrograde irrigation) into the nasolacrimal duct or alternatively into the upper or lower puncta and respective canaliculus (antegrade irrigation). This author prefers to use a 3.5 Fr Tom Cat catheter (Kendall Co., Mansfield, Mass.). Sterile saline or water (5-10 ml) is then irrigated by applying gentle pressure to the syringe plunger while applying digital pressure to the nasal punctum to prevent fluid reflux. Fluid should flow from the upper and lower lacrimal puncta. Patency of each respective punctum may be evaluated by applying gentle digital pressure to the upper and then the lower punctum during irrigation. If the nasal punctum in the nasal vestibule is absent, the floor and medial wall of the nasal vestibule should be palpated digitally for a fluctuant swelling (representing a distended segment of the nasolacrimal duct) while an assistant irrigates through the upper or lower eyelid lacrimal punctum.

Mucopurulent and purulent ocular discharges should be collected and submitted for bacterial culture and susceptibility testing and, if suspected, for fungal culture. Samples should be collected before topical anesthetic is instilled. Cytologic examination of ocular discharge is performed infrequently.

When catheterization and irrigation of the nasolacrimal system does not alleviate the obstruction and result in patency of the nasolacrimal duct, contrast dacryocystorhinography is indicated. Injection of an iodine-based contrast agent into the nasolacrimal system may assist in localization of nasolacrimal duct obstruction. Dacryocystorhinography may be done with plain film radiography or fluoroscopy. The horse is sedated, and the nasolacrimal duct is irrigated with 0.5% proparacaine HCl. General anesthesia may be required to obtain satisfactory radiographs. Survey radiographs are made from lateral and oblique views to provide the best visualization of the duct and to minimize summation tissue artifact. The lacrimal punctum of the upper eyelid is then cannulated, and 5 to 20 ml of contrast medium is injected. Radiographs are then made (or fluoroscopy repeated) to identify the site of obstruction.

Direct imaging of the nasolacrimal system is possible by videodacryoscopy with a 0.7-mm to 2.8-mm (external) diameter microendoscope. The advantage of videodacryoscopy is direct imaging of the site of obstruction and its being a minimally invasive diagnostic procedure. However, cost limits its widespread use.

TREATMENT

Disorders that cause excessive lacrimation (ocular pain or irritation) should be identified and treated appropriately. A complete nasolacrimal obstruction that is located in surgically accessible location is generally amenable to treatment. Obstruction that results from severe fulminant trauma or neoplasia of surrounding tissues may not be treatable; the practitioner should consult with the owner and realign any unrealistic expectations associated with the given diagnosis.

When the distal nasolacrimal duct is dysgenic or when gentle pressure during irrigation does not result in establishing patency of the nasolacrimal duct, a catheter may be advanced to the site of dysgenesis or obstruction. A sterile urinary catheter (size 5-8 Fr), red rubber feeding tube of the same size, or a polyethylene tubing (PE 160-200) may be inserted into the upper or lower lacrimal puncta and advanced gently until resistance is encountered. In most young horses with atresia of the nasal punctum inside the nasal vestibule, simply excising the mucosa overlying the catheter tip will establish patency. Placement of a retention catheter is not necessary, and treatment with topical antibiotic solution is recommended for 10 days. When dysgenesis of a greater portion of the distal nasolacrimal duct is present and the tip of the catheter is still palpable beneath the mucosa in the nasal vestibule, a mucosal incision may be made over the end of the catheter to expose its tip. The catheter tip is then advanced through the mucosal opening and secured with sutures to the inside of the nostril. Alternatively, an incision may be made through the false nostril; the catheter is passed through it; and it is sutured to the facial skin above the nostril. The catheter should remain in place for 3 to 8 weeks to prevent stricture and ensure patency. Topical ophthalmic antibiotic solution is recommended while the retention catheter remains in place.

When atresia, dysgenesis, or obstruction occurs proximally to the area accessible inside the nostril and the catheter tip cannot be palpated, the catheter should *never* be forced through the site of obstruction. A substantial

vascular supply exists at the rostral extension of the ventral nasal concha, and excessive hemorrhage may occur if a catheter is forced into or through this location. Continuous, gentle irrigation alternating just proximally and just distally to the site of obstruction may alleviate the obstruction and result in patent nasolacrimal drainage. Obstructions that are not accessible inside the nostril should be referred for evaluation and treatment. Treatment includes videoendoscopic laser treatment or conventional surgery to create an alternate pathway for drainage of tears.

Although uncommon, stenotic lacrimal puncta may be corrected surgically by simply enlarging the punctal diameter with the use of scissors. Ectopic lacrimal punctum may be treated in the same manner as for stenotic puncta.

Supplemental Readings

- Barnett KC, Crispin SM, Lavach JD et al: Examination of the eye and adnexa. In Barnett KC, Crispin SM, Lavach JD et al: *Color Atlas and Text of Equine Ophthalmology*, pp 19-21, London, Mosby-Wolfe, 1995.
- Dziezyc J: Nasolacrimal system. In Auer AJ (eds): *Equine Surgery*, pp 630-634, Philadelphia: WB Saunders, 1992.
- Harling DE: Epiphora and lacrimal dysfunction in the horse. *Equine Pract* 1988; 10:27-38.
- Lavach JD: *Large Animal Ophthalmology*, St Louis, Mosby, 1990.
- Moore CP: Ocular discharge. In Robinson NE (ed): *Current Therapy in Equine Medicine*, 3rd edition, Philadelphia, WB Saunders, 1992.

SECTION X

Musculoskeletal Disease

Edited by Dr. Christopher E. Kawcak

CHAPTER 10.1

Orthopedic Concerns in the Prepurchase Examination

DANIEL MARKS
Santa Fe, New Mexico

This chapter deals with orthopedic considerations in the prepurchase examination of sport horses (i.e., jumpers, eventers, hunters, and dressage horses) and Thoroughbred flat and steeplechase racehorses. The purpose of the examination is to detect and, when possible, diagnose actual or potential problems and consider their significance in relation to the horse's intended use.

WORKSHEET

A worksheet (Figure 10.1-1) can serve the following purposes:

1. A checklist of points to be inspected
2. A record of all findings
3. A record of limitations of the specific examination
4. A contemporaneous legal document
5. A source in generating the report to the buyer

The worksheet is not given to the buyer and is not a prepurchase report.

HISTORY

Specific questions about the horse's veterinary and medication history are asked of the seller or their agent. In the past these questions might have been considered inappropriate. However, neglecting them may place the veterinarian at a medical disadvantage or even in legal jeopardy. This author believes that the veterinarian should only comment on medical aspects and safety and not on suitability. The seller/agent is required to sign the history; if the footing is precarious for the horse, this individual should also sign a release.

OBSERVATION OF THE RESTING HORSE

It is usually good policy to have the seller or their designee lead, lunge, and ride the horse, unless the rider for the buyer has good sensitivity that can help detect subtle problems. If such a rider has previously ridden the horse, their comments are solicited.

The first few steps the horse makes from its stall are observed, with special attention given to hoof landing. Toe-walking may only be evident at this time. The horse should stand square on a level surface with good lighting. Muscle atrophy is regarded relative to the general muscling. For instance, a well-muscled horse with prominent lumbar vertebral spines may have epaxial atrophy secondary to back pain, trapezius atrophy suggests a poor-fitting saddle, and quadriceps atrophy, which is best assessed during a hock flexion test, can indicate stifle pain. On the other hand, muscle hypertrophy can be compensatory, as with gluteal hypertrophy from chronic laminitis. Palpation can be used to identify heat, pain, symmetry, tissue compliance, and asymmetry. Manipulations can be used to evaluate range of motion and accentuate pain. The horse must be relaxed to evaluate painful responses both standing and in motion; if this cannot be achieved with horsemanship, then a tranquilizer may be necessary. The seller/agent must give permission, and samples for drug testing should be obtained first.

CONFORMATION

Conformation that relates to athletic ability is outside of the scope of the examination; however, abnormalities that might relate to soundness are recorded. Slight variations that have little clinical significance should be covered in the report to the buyer. For instance, if a horse has been

☐ Buyer/Rider Professional Advanced amateur Some experience Novice Intended use.....
☐ Export? N/Y/Maybe Intend to breed? N/Y/Maybe Insurance exam N/Y..... Form N/Y
☐ HISTORY Per: Seller/Agent/Trainer/Rider/Barn manager.....
 Intended use..... How long horse has been in your care..... Last shod.....
 Work last month..... Last 3 days..... Today..... Last competed / /
 Usual medications before or after competition N/Y.....
 MEDICATIONS (not by vet) in past month N/Y.....
 FEED (e.g., special feed, wet hay, supplements, etc.) N/Y.....
 Regular veterinarian(s) for horse.....
 Veterinarians for stable.....
 VETERINARY exam, treatment past 6 months (e.g., sick, lame, inject: joint, nerve, back) / / Dr.
 X-rays, Ultrasound, Nuclear scan N/Y/NK Date: / / Per Dr. Location:
 Purpose.....
 Why?.....
 SURGERY (e.g., colic, joint, throat, hock, stifle, tendon, desmotomy, nerved, etc.) N/Y/NK..... Dr.
 QH blood, Impressive N/Y/NK; Arab CID lines N/Y/NK; P. Paso parents suspensory N/Y/NK.....
 VICES Biting, Striking, Kicking, Rearing, Bucking hard, Head-shaking, Cribbing, Wind-sucking Other N/Y.....
 Is there anything else you know about this horse as regards safety that might influence the sale? N/Y.....

☐ To the best of my knowledge the above statements are correct: / /
 Because the going is..... and not ideal, I accept any risk to the horse and/or rider that may occur during the course of the examination.....

☐ PEOPLE PRESENT AT EXAM.....

☐ GENERAL CONDITION Coat E G F P Muscling E G F P Fat..... Thin
☐ CONFORMATION Withers Low..... High..... TS NR.....
☐ M-S Weather NR Wet Icy ☐ TMJ NR L..... R..... POLL NR L..... R..... NECK NR L..... R.....
 BC NR L..... R..... Pec NR L..... R..... Tri NR L..... R..... Lats NR L..... R.....
 Trap NR L..... R..... Serr NR L..... R..... Pec NR L..... R..... Oblique Ab NR L..... R.....
 TFL NR L..... R.....
☐ Back NR.....
 Cycle NR..... Manip N/Y.....
 S-I NR..... Sacrum NR..... Tuber coxae L NR..... R NR.....
 Pelvis NR..... Gluts L NR..... R NR.....
 Hams L NR..... R NR.....

☐ LF ☐ Neurectomy ☐ Digital pulse Flexion and rotation NR..... Inactive medial splint NR ☐ Testers
 Percussion.....
 Front shoes..... Wear NR.....

☐ RF ☐ Neurectomy ☐ Digital pulse Flexion and rotation NR..... Inactive medial splint NR ☐ Testers
 Percussion.....
 Wear NR.....
☐ LH ☐ Patella, desmotomy Lat dig flex Cunean tenectomy Gastroc MT pulse Digital pulse
 Splint test CT..... ☐ Testers NR
 Stifle NR.....
 Hind shoes: Wear NR.....

☐ RH ☐ Patella, desmotomy Lat dig flex Cunean tenectomy Gastroc MT pulse Digital pulse
 Splint test CT..... ☐ Testers NR
 Stifle NR.....
 Wear NR.....

☐ In Hand Going..... Walk NR.....
 L circ NR Abduct RH Crossing..... Front.....
 R circ NR Abduct LH Crossing..... Front.....
 Backup NR.....
 Trot LF..... RF..... LH..... RH.....
☐ LFF NR..... L carpus NR..... RFF NR..... R carpus NR.....
 LH flexi NR..... LHF NR..... LHR NR.....
 RH flexi NR..... RHF NR..... RHR NR.....

☐ Lunge/Lead going..... L circ NR.....
 R circ NR.....

Figure 10.1-1 Example of a worksheet used in prepurchase examination. N, No; Y, yes; NK, not known; NR, not recorded; E, excellent; G, good; A, average; P, poor.

Hill N/Y Walk Up..... Down.....
Trot Up..... Down.....

Percuss N/Y LF..... RF..... Toe up N/Y LF..... RF.....
Testers N/Y LF..... RF.....

☐ RIDING Rider..... Tack NR..... Going.....
☐ Saddling and mounting NR.....
Carriage NR.....
Walk NR..... Reinback NR.....
LF..... RF..... LH..... RH.....
L circ.....
R circ.....
LH Diag NR..... RH Diag NR..... Fig 8 LtoR NR.....
RtoL NR.....
Ext trot N/Y NR.....
L Canter NR..... Small NR.....
R Canter NR..... Small NR.....
Gallop L NR..... R NR.....
Changes N/Y LtoR NR..... RtoL NR.....
Other.....

☐ SHOES OFF Sole, White line LF NR..... RF NR.....
☐ Testers L..... R..... Going.....
LF..... RF..... LH..... RH..... L circ.....
R circ.....

☐ X-RAY EXAM Front feet..... MCPJ..... Prox MCIII..... Carpus..... Stifle..... Hock..... MTPJ.....
Back..... Other.....
Dr.

☐ RADIOGRAPHIC INTERPRETATION: E G A P ND = Not Diag, U = Under, O = Over, M = Motion

☐ Ultrasound N/Y.....
Scintigraphy: Thermography, Other.....

Figure 10.1-1, cont'd For legend see opposite page.

fulfilling its athletic requirements for some years without signs of a problem, a conformation defect has less significance than in an untested horse. The following should be mentioned in the report to the buyer:

1. A defect that will likely affect the eventual soundness of the horse in relation to a specific discipline (e.g., a slight "back-at-the-knee" conformation is significant in a racehorse but not in a hunter)
2. A particular conformation that might accentuate a clinical or radiographic finding (e.g., "toed-in" forelimb conformation may accompany a lateral suspensory branch lesion)
3. Any conformation defect if the intended purpose for the horse is a competition that is judged on conformation
4. Any obvious conformation defect, even if it is unlikely to have an effect on future soundness (e.g., over at the knee)

CLOSE OBSERVATION AND PALPATION

The lateral surfaces of the temporomandibular joints and all palpable muscles are palpated for pain. For instance, deep pain in the middle gluteal may signify a gluteal myositis/tendinitis, whereas pain in the brachiocephalicus is usually secondary to lameness. Specific cutaneous points that relate to painful joints are also evaluated. The neck is palpated, with emphasis on the dorsolateral muscle group and is bent to the girth to evaluate range of mo-

tion or discomfort. The external curvature is observed for flat spots, indicting stiffness. If heat or pain over a joint facet exists, radiography should be considered.

Kyphosis ("roach back") sometimes denotes back pain, which can be caused by bilateral stifle soreness, or may be a normal conformational variation. Lordosis ("sway-back"), unless painful, is frequently functional. The examiner can discern scoliosis, which can be spastic or functional, by viewing the horse from above. Hair worn off a 2- to 5-cm circle under the rear of one or both saddle panels might signify a poorly fitting saddle, but with pain and concomitant muscle splinting, even well-fitting saddles can rub the hair excessively. During the back examination, the horse's head is turned slightly so that the examiner can observe its facial expression and flattened fingers are gently rubbed over the dorsal midline from the withers to the tail to reassure and relax the horse and help to detect increased heat, swelling, scars, or bony enlargements.

The horse's reaction to palpation, whether splinting, collapsing, bucking, or kicking depends on the amount of tenderness present and the horse's personality. With experience, a distinction can usually be made between normal reflex withdrawal and a painful reaction. Edema on the midline, especially on the cranial lumbar spines, may result from saddle bruising or supraspinous ligament damage. However, insensitive hard swelling in this region is usually insignificant. The tail should be manipulated for tone and pain. The examiner should also palpate the dorsal spines from withers to tail using firm digital pressure (4.5 kg) with the finger pads while moving the hand

caudally. Any sensitive areas should be skipped and palpated last to avoid apprehensive guarding. The longissimus dorsi muscles are examined by gentle palpation with the flat of the fingers. This motion is repeated more forcefully to evaluate muscle compliance and pain. If the horse has been in work and shows a painful response to palpation on the midline, soreness of the adjacent epaxial muscles is usually present. Thoracolumbar spinal pain also appears to cause an interrelated reaction to firm pressure (5 kg) over the dorsal processes of the sacrum. Cranial thoracic pain usually causes sensitivity over the cranial sacrum and more caudal thoracic or lumbar pain evinces sensitivity along the caudal sacral midline. Sacroiliac pain usually manifests in a painful reaction to squeezing across the tuber sacrale (with the thumb and opposing finger about 4 cm from the dorsum and 10 kg of pressure), accompanied by pain on deep palpation (5 kg of pressure) at the lumbosacral space. The horse may demonstrate a reluctance to flex the lumbosacral joint, and in chronic cases, the horse may exhibit an excessive excursion of both tuber coxae when trotting.

The horse is encouraged to repeatedly cycle its back through utmost flexion (ventroflexion and roaching) and extension (dorsiflexion and dipping). The examiner accomplishes flexion in the horse by firm digital pressure over the caudal sacral midline; by squeezing the tailhead; by pushing up on the abdomen; or by bilateral pressure applied over points in the caudal biceps femoris coxae muscle. Extension is accomplished by digital pressure over the longissimus muscles. If the horse repeatedly cycles its back with no significant discomfort, the likelihood of serious spinal disease is minimal. However, if the horse cycles once and then refuses to repeat or if it displays pain, disease is suspected. The examiner evaluates lateral flexibility by running a blunt point caudally along each epaxial muscle. Considerable individual variation exists in the flexibility of the spine, and unless extremely reduced, range of motion is difficult to judge. Hunters and low-level jumpers can function with some back pain, but moderate back pain is inconsistent with high-level jumping or dressage.

FORELIMB EXAMINATION

With the horse's leg weight-bearing, pressure applied over the bicipital tendon/bursa should be painless. The examiner can evaluate carpal joint distention by applying pressure on the dorsum of the joint, which is reflected in the lateral palmar pouches. If distention in the carpal sheath extends proximal to the carpus, a carpal canal problem could be present. Palpation of the flexor tendons and suspensory ligament (SL, also referred to as *interosseous muscle*) is especially critical because significant lesions can exist that do not cause lameness; however, ultrasound examination of any suspect lesion is warranted. Running the side of the index finger along the palmar surface of the superficial digital flexor (SDF) tendon with a force of approximately 2.5 kg should be painless to the horse. The tendons and branches of the SL should be palpated for heat, size, contour, and their relative tensions. The tensions in the SDF and SL should be equal; however, the deep digital flexor (DDF) should be slightly less taut. Distention of the digital sheath with little pressure is usually

insignificant. However, substantial effusion often indicates tenosynovitis, especially if the distal pouch between the annular ligaments of the pastern is firmly distended. Notching of the SDF proximal to the fetlock often indicates annular ligament constriction.

The superior check ligament should be palpated with the horse's limb raised. The carpus should be flexed for range of motion, and while the horse's foot is held between the examiner's knees, the dorsal margins of the joints should be palpated. The flexor tendons and SL should be gently examined for size, shape and compliance, and firmer pressure should be used to elicit pain. Rounding of the edges of the SDF is a subtle but significant finding that calls for ultrasound examination. The SL is normally the most reactive to squeezing because hard work often transiently increases SL sensitivity with no lameness or structural damage. Firm thumb pressure applied over the SL origin may elicit pain; however, the medial side is normally less reactive than the lateral. The splint bones should be examined, and in racehorses, the dorsum of the third metacarpal bone should be palpated for bucked shins or stress fractures. To evaluate the insertion of the SL branch, the examiner applies firm thumb pressure over the apex of the sesamoid bone and then passively cycles the metacarpophalangeal joint. The bases of the sesamoids are similarly checked. The annular ligaments of the pastern, the branches of the SDF, oblique distal sesamoidian ligaments, and DDF tendon should also be assessed.

HINDLIMB EXAMINATION

The region over the greater trochanter should be palpated for pain, which is usually secondary to a lower leg problem. The stifle should be palpated for fluid pressure and the medial collateral ligament and edge of the medial meniscus should be pressed firmly; this does not normally elicit pain. With the leg slightly unweighted, strong (12 kg) caudal intermittent pressure should be applied to the patella so as to make it slide along the trochlear ridges. If pain is coupled with crepitus the prognosis for jumping or collection is often poor. The Achilles tendon should be examined. Tarsocrural joint effusion (bone spavin) and medial swelling (bone spavin or sign of cunean tenectomy) should be evaluated. With the horse's leg slightly flexed the cunean tendon should also be palpated; this should be painless.

EXAMINATION OF THE HORSE IN MOTION

Throughout the examination the horse's reactions (facial expression, tail carriage, and body language) should be noted for signs of discomfort. Movement in hand should be on a level, hard surface (packed dirt or nonslip asphalt are ideal). Some horses are apprehensive and will not stride out on a hard, smooth surface, which should be avoided for safety.

The following should be noted:

- A head bob or merely a tightening of the neck muscles
- Asymmetric movement of the tuber coxae

- Flattening of the middle gluteal muscle
- The flight of each leg as viewed in two planes

The examiner should also note the occurrence of breakover, the relative amount of retraction and protraction, the hoof direction before grounding, hoof landing pattern, overstep at the walk and trot, hind hoof rotation during late stance, and fetlock translation. Some lameness is more apparent at the walk because less momentum exists to carry the leg to full protraction, and the leg lacks the loading to provide elastic rebound. The amount of overstep should be consistent with the horse's conformation and the speed of the gait, and is best observed in sand. Very small, slow circles should be made in both directions, which can elicit pain from limb torsion, difference in lateral back flexibility, and/or neurologic dysfunction. The horse should be backed in hand and compared with a rein-back when ridden. The horse should be trotted in hand slowly as well as fast. When the horse walks and trots up and down a grade some lameness such as forelimb-high suspensory disease, or intermittent upward fixation of the patella, may be exaggerated.

Flexion tests should be performed before the horse's lunging is assessed. Range of motion and any discomfort when flexed are noted. The metacarpophalangeal and interphalangeal joints should be flexed with a force of 11 kg for 30 seconds. This author tends to ignore the first couple of steps; however, persistence of lameness is noted. A positive test with no other clinical or radiographic signs may be inconsequential. The carpus should be flexed for 1 minute; lameness may implicate the carpus, carpal canal, or, infrequently, the elbow. The entire hindlimb should be flexed for 90 seconds. A positive response is typically indicative of a problem. A positive reaction may then be followed by selective flexion tests. A hind leg retraction test (in which the horse's leg is pulled caudally for 90 seconds), after which the horse is jogged can exaggerate some stifle and extensor component pain.

Observation of the horse lunging on a hard, nonslip surface is the best way to see most lameness; however, deep going may exaggerate lameness such as forelimb high suspensory disease. Observation of the canter should focus on the degree of lateral separation between the hind legs, the amount of pastern translation, and the proportion of total weight carried by the hind legs. Back stiffness or neurologic disease can cause the impression of a loss of connectedness between the front and hind ends.

RIDING

The horse should be ridden as for its intended purpose. For example, a grand prix dressage horse should demonstrate all the movements. First, all three gaits are demonstrated in a relaxed natural balance. If the horse does another basic gait (e.g., rack, slow gait, or running walk) this too is observed. The horse's movement should be compared with lunging because some lameness is exaggerated by the weight of the rider.

Back soreness is often manifested by the horse raising its head in a constrained manner, an uncomfortable facial expression, a lack of hind engagement, and/or a lack of connectedness between front and hind ends. The rider

may feel unilateral or bilateral longissimus rigidity. The rider can ride the horse with a soft seat and then stiffen his back, sitting hard, to see if this appreciably changes the horse's behavior. If the saddle is the culprit, the rider standing in a two-point position or sitting back on the cantle to change the pressure from the saddle may change the horse's carriage and way of going. Some horses that jig and refuse to walk will immediately revert to a good walk with such a change. A rein-back is often impaired by cranial thoracic pain and neurologic disease.

A number of movements are helpful in the observation of lameness. In posting trot the rider should change diagonals every ten steps on a straight line and on both circles. The rider may feel and the examiner may observe a difference, because the lame hind leg often will not push off as strongly; therefore the rider will not be thrust up as much. The lameness may be intensified and the horse's expression may change with change of diagonals. In sitting trot the rider should make small (6-m circles) figure-eights with a very abrupt change of direction between circles. This motion forces the horse to step to the side for a couple of strides to keep its balance and will exaggerate some front and hind lameness. In canter the rider should have the horse gradually tighten the circle until it cannot go smaller. Flying changes, which are degraded by hock and stifle soreness, should also be observed.

The horse should be galloped (at approximately 18 mph, 500 m/min) around reasonably tight turns in both directions. Cross-galloping, excessive shortening of the stride, inappropriate lead changes, and/or decrease in lateral hind separation may indicate pain, and restriction to scapular rotation is more evident in an extended canter. Extended trot may be uneven because of a forelimb high suspensory ligament disease, half passes often accentuate femorotibial joint lameness, and zigzags often accentuate back soreness. The author usually does not watch the horse jumping unless the examination suggests a need or the buyer has a concern about the jump (e.g., the horse drifts, twists, or is more comfortable on one lead.) Usually a horse jumps away from a sore front and toward a lame hind leg because of the uneven hind leg push.

IMAGING

The horse's front shoes should be removed before radiography and wear on the sole (upper) surface of the shoe should be noted. The sole and white line should be inspected and the horse should be jogged barefoot. The following radiographs are routinely taken as survey films for superior sport horses and may be augmented according to clinical findings:

1. Front foot—Five views are taken. The anteroposterior (AP) view is angled down 30 degrees and two dorsoventral views are taken for the navicular and third phalanx (P3). The dorsal wall should have a marker on the lateral view to show any rotation and to measure the wall thickness.
2. Metacarpophalangeal joint—Three to five views are taken.
3. Third metacarpal bone—The AP is exposed to visualize proximal sclerosis that may suggest a high suspensory desmopathy.

4. The carpus usually is not viewed unless the horse has recently raced or clinical signs warrant it.
5. Hind fetlock and pastern—Two to five views are taken.
6. Hock—Four views are taken. The AP should be slightly overexposed to evaluate any sclerosis of the metatarsal bone.
7. Stifle—Three views help demonstrate the lateral trochlea, tibial plateau, and medial femoral condyle.

For racehorses the following views are added:

1. Carpus—A full series of films is taken, including skyline and flexed lateral views.
2. Third metacarpal bones—A lateral view helps rule out stress fractures.
3. Metacarpophalangeal joint—Five views are taken, including a flexed lateral
4. Front foot—The navicular view may be omitted, but dorsoventral oblique views may be added to image wing fractures.

LESIONS

Navicular disease is a clinical diagnosis that includes evidence of lameness, and radiographs sometimes do not correlate with clinical signs. European warmbloods tend to have more prominent synovial fossae in the distal border than do Thoroughbreds. This characteristic should not be considered pathologic; however, the shape of the proximal border has been shown to correlate with navicular disease. Certain radiographic lesions are of serious concern. These include multiple large circular or ovoid lucencies; a large central, poorly marginated radiolucency, which is usually associated with adhesions to the flexor tendon; evidence of a full cortical defect, as seen on the skyline view; and well-defined cysts that may remain clinically silent but if they collapse, can result in severe lameness. Some horses with mild navicular disease, if they are shod and managed well, are acceptable for pleasure riding and easy competition, but show jumping is usually not compatible with navicular pain. Dressage riding surfaces are forgiving of foot problems, but a tendency to shorten stride may not be acceptable. Corners, zigzags, and extended trot are movements in which navicular disease is likely to affect performance. Hunters can compete with mild navicular disease provided that the horse's natural gallop stride is long and the going not too hard.

Ossification of the collateral cartilages (sidebones) is frequent, especially in horses with draft blood. These ossifications almost never cause lameness, nor do asymmetrical ossifications relate to uneven foot loading.

Radiographic lucencies or irregularities of the distal border of P3 that have been termed *pedal osteitis*, are often inconsequential in clinically normal horses. Small marginal fractures of the dorsal border may cause lameness or hoof tester reactivity, but can usually be managed by shoeing.

Radiographically demonstrable distal interphalangeal degenerative joint disease (DJD) is serious, as can be a large irregular fragment of the extensor process. A small, smooth density is usually benign, however. Radiographic

evidence of articular osteophytes in the proximal interphalangeal joints of both front and hind legs are common (especially in warmbloods) and may be of no consequence. However, the possibility that this is a precursor of DJD should be considered.

The following radiographic findings in the fetlock joints are usually associated with sensitivity to forced flexion and a positive flexion test, and are cause for concern:

- Palmar subchondral lysis
- Full-thickness cartilage loss at the transverse ridge (gull wing lesion)
- Large enthesiophytes of the sesamoid apex or base
- Sesamoid fractures
- A very pronounced dorsal notch of the dorsodistal cannon bone (villonodular synovitis)
- Large dorsal or palmar/plantar P1 fragments

On the other hand, small, rounded radio-opacities on the dorsal border of the joint, flattening of the palmar condyle of metacarpal-3 (MCIII), vascular channels in the sesamoid bones, or signs of healed capsulitis are frequently benign. In racehorses, sesamoid lucencies are more likely to lead to sesamoid fractures, but with sport horses this problem is very rare.

Carpal joint disease is infrequent in sport horses with the exception of cutting horses. Radiographic evidence of remodeling that would prejudice racing may be acceptable in a jumper if the joint is clinically quiet. Radiographic evidence of a fibrous union in a healed accessory carpal fracture, with a normal carpal sheath, is usually insignificant. Jumpers sometimes incur direct trauma to the dorsum of the carpus and extensor carpi radialis tendon. This type of impact can tear the retinaculum and cause a bursal enlargement. If no limitation exists to range of movement or pain with flexion and palpation, the defect is likely just cosmetic.

Medial front splints are customary and usually insignificant. Axially misaligned forearm and cannon (bench knee) predispose to medial splints. Palpable splint soreness, without overt lameness, may affect jumping, and some lateral splints heal slowly and may cause protracted lameness. Visually evident splints detract from a conformation hunter, and flared or fractured distal splint bones are common in racehorses (harness racehorses experience a very high incidence), and are usually associated with chronic suspensory ligament branch desmitis, which is of concern.

Suspensory apparatus damage is very frequent in sport horses. Front leg high suspensory disease (HSD) is common, but jumpers with mild front leg HSD, surprisingly, can compete satisfactorily over big fences, usually with little or no increase in the lameness. Dressage horses with mild HSD that warm up out of the lameness can compete unless the horse shows unevenness in the corners or extended trot. Unlike front HSD, hind HSD can seriously detract from advanced jumping and dressage, and is usually associated with a straight hock. Radiographic evidence of cannon bone sclerosis is associated with more severe HSD and is more common in the hind leg.

Front or hind suspensory branch lesions are frequent in sport horses and should be evaluated cautiously. If the damage extends to the sesamoid attachments the progno-

sis is often poor. However, there does not seem to be any correlation between sesamoiditis and the prognosis for branch injuries. Stretching the suspensory ligament that permits increased pastern translation, which is best appreciated in motion, can lead to progressive debility, and is worsened by straight hocks and sloping pasterns. Although this problem usually develops in older broodmares, it can affect horses in their prime and is usually career ending. Suspensory ligament body tearing often heals with substantial thickening and decreased elasticity, which may be suitable for hunters, but usually does not hold up for show jumping, racing, or dressage.

Radiographic evidence of oblique distal sesamoidian ligament or superficial digital flexor desmopathy is common and not necessarily disqualifying, but may indicate the need for further evaluation by ultrasonography. Ultrasound assessment is especially needed if avulsed fragments are evident or the structures palpate abnormally. Superficial digital flexor branch lesions are frequently associated with more proximal tendinitis, which offers a poorer prognosis than a healed branch.

Healed superficial digital flexor tendinitis (bowed tendon) is usually tolerable for sport horses, except for 3-day eventers in which there is a strong tendency for recurrence. However, with time and treatment the horse may compete again. Sprinting racehorses have the poorest prognosis.

The most frequent area for front and hind DDF tendon damage, including longitudinal tears, is within the digital sheath. Healing is very slow and there is a tendency for adhesion formation, which implies a poor prognosis. Thickening of the digital annular ligaments of the pastern can accompany severe DDF pathology and any thickening secondary to navicular disease is disqualifying.

Inferior check ligament desmitis is common in jumpers and dressage horses, and is usually denoted by a thickened ligament. Once healed most do not cause problems.

Stifle soreness is common in athletic horses. Obvious femoropatellar effusion associated with prominent osteochondrosis dissecans (OCD) of the trochlea is a cause for concern. Most painful femorotibial joints are radiographically negative, but ultrasonography is valuable for diagnosing meniscal damage, which is usually progressive and serious.

Soreness of the distal hock joints will affect a majority of all grand prix jumpers and dressage horses and is common in other sport horses and racehorses. This usually requires treatment to maintain peak performance. The correlation between mild radiographic evidence of remodeling and clinical findings is not good, but severe changes are meaningful. Fused joints are usually pain free, although this rarely occurs unaided. Angulated hocks with a narrow lateral dimension and a suggestion that the bend of the hock is carried through the distal joints are often unsuitable for demanding collection. Distention of the tibial tarsal joint most commonly results from osteochondritis dissecans (OCD) and although most cases do not affect performance, large pieces can cause soreness and require surgery.

Occasionally the hind superficial DDF tendon undergoes avulsion from the tuber calcis. This injury occurs in jumpers and racehorses and, more frequently, in eventers and chasers. The tendon usually luxates laterally, and occasionally horses retain a slight mechanical lameness. Some have returned to compete successfully at a high

level in jumping and eventing. However, racehorses do not appear to attain their previous level of performance. Some warmbloods are prone to an enlargement of the lateral digital extensor tendon sheath just distal to the hock, which is functionally insignificant.

Stringhalt or shivering is not compatible with dressage performance, but affected jumpers have performed successfully for years with no obvious progression of signs. "Shivers" or "shivering" usually occurs in large half-breeds, and may be a form of polysaccharide storage disease, which is genetic. A muscle biopsy is required for a definitive diagnosis.

DRUG TESTING

Drug testing protects the seller and buyer. The author always gives warning that the examination will require a drug test, and that both urine and blood samples should be submitted.

VIDEO RECORDING

Parts of the examination can be documented with a still camera, or even better, a video camera. Gait abnormalities can be studied in slow motion and can be viewed by colleagues for additional opinions. Conformation and condition are recorded for legal purposes and can serve as a baseline for comparison with future findings.

SUMMARY

The purpose of the examination is to furnish the prospective buyer with medical information that is germane to the decision whether or not to buy the horse. The examination does not certify soundness, nor does it guarantee the horse. Black or white findings are not usually a problem; it is in the interpretation of the gray areas that is where the experienced practitioner can make an informed appraisal of the current medical status and the probable implications of these findings relevant to the horse's intended occupation.

Supplemental Readings

- Anderson GF: Evaluation of hoof and foot relevant to purchase. *Vet Clin North Am Equine Pract* 1992; 8:303-318.
- Dyson SJ: The prepurchase examination. In Mair TS (ed): *Evaluation of the Musculoskeletal System*, Newmarket, England, British Equine Veterinary Association, 1998.
- Goble DO: Medical evaluation of the musculoskeletal system and common integument relevant to purchase. *Vet Clin North Am Equine Pract* 1992; 8:285-302.
- Marks D: The prepurchase examination of jumpers and dressage horses. *Proceedings of the 45th Annual Convention of the American Association of Equine Practitioners*, 1999.
- Poulos PW: Radiographic evaluation of the horse relevant to purchase. *Vet Clin North Am Equine Pract* 1992; 8:319-328.
- Reid C, Raker C, Marks D et al: The soundness examination: clinical and radiographic findings, their correlation and legal implications. *Proceedings of the 20th Annual Convention of the American Association of Equine Practitioners*, 1974.

original equipment for performing nuclear scintigraphy was expensive and only available in academic environments. Because prepurchase examinations are more commonly done in private practice, nuclear scintigraphy has not been able to demonstrate its worth as a tool in the prepurchase examination. Another reason for its absence from the prepurchase examination may be that it is a relatively invasive technique compared with radiology. The horse must be injected with the radioactive compound and stay in the veterinary facility overnight according to local radiation safety laws. Although this is not a problem for a routine lameness case, it can be when the prospective owner instead of the current owner requests the examination. Finally, the cost of nuclear scintigraphy may discourage some clients from requesting it as part of the prepurchase examination.

Inclusion of nuclear scintigraphy in the process of the prepurchase examination will undoubtedly raise some important issues regarding interpretation. It will still be the duty of the veterinarian who performs the examination to determine the significance of any regions of IRU detected. In some areas IRU would not be considered conducive to

future athletic performance, for instance, focal and intense increased navicular bone uptake and any focal and intense IRU around a joint such as the carpus, fetlock, shoulder, or stifle. Conversely, some areas of IRU that might be less important to the prospective buyer are the distal hock joints or splint bones. Referral for prepurchase nuclear scintigraphy has great potential, but, as with all its other uses, radiographic screening must be interpreted in light of the physical examination and gait evaluation.

Supplemental Readings

Chambers MD, Martinelli MJ, Baker GJ et al: Nuclear medicine for diagnosis of lameness in horses. *J Am Vet Med Assoc* 1995; 206:792-796.

Dyson S, Martinelli MJ, Pilsworth R et al (eds): *Equine Scintigraphy*, Newmarket, England, *Equine Vet J* (in press).

Hoskinson JJ: Equine nuclear scintigraphy: indications, uses, and techniques. *Vet Clin North Am Equine Pract* 2001; 17(1):63-74.

Twardock AR: Equine bone scintigraphic uptake patterns related to age, breed, and occupation. *Vet Clin North Am Equine Pract* 2001; 17(1):75-94.

CHAPTER 10.3

Thermography

TRACY A. TURNER
Saint Paul, Minnesota

Thermography is the pictorial representation of the surface temperature of an object. This noninvasive technique that measures emitted heat and represents the surface temperatures of skin is a useful method to detect inflammation. The ability to noninvasively assess inflammatory change makes thermography an ideal imaging tool to aid in the diagnosis of certain lameness conditions in the horse.

First used in veterinary medicine 35 years ago, the use of thermography has been mostly limited to university hospitals and large referral practices. In the last 20 years, however, thermography has been put to practical use in equine medicine.

INSTRUMENTATION

In the past, thermographic instrumentation has been divided into two categories—contacting thermography and noncontacting thermography. Contacting thermography uses liquid crystals in a deformable base. The crystals change shape according to the temperature that contacts them and in the process they reflect a different color of light. Therefore the color of a crystal represents a specific temperature. To use this technology for medical purposes, the liquid crystals are embedded into a flexible and durable latex sheet. This

method has fallen from favor because of numerous inherent problems in applying the technology that have made noncontacting thermography the method of choice.

Two different technologies for noncontacting thermography exist—cooled and uncooled. Cooled technology uses an infrared radiation detector to measure temperature. In addition, a series of focusing and scanning mirrors are used to systematically measure an entire field of view. The camera/detector is usually coupled to a cathode-ray tube and the intensity of the detected radiation is converted to an electrical signal. This signal is displayed on the cathode-ray tube as a black-and-white (gray scale) image of the object that is directly proportional to the gray scale. Through the use of microchips, the black-and-white image can be made into a colored image of the thermal picture; hence a classic thermogram is generated. Because of the heat generated by the camera, the detector must be cooled to prevent interference. The complexity of the camera makes this equipment expensive, and furthermore it requires attachment of a computer, which makes it difficult to transport. Uncooled technology uses a type of focal plane array in which infrared radiation is focused and measured on a series of detectors.

Several factors should be considered before a thermographic camera is purchased. Among the most important

Table 10.3-1
Internet Addresses for Equine Thermography Instruments

Instrument	Website
CEPID Instrument Systems	http://www.cepid-infrared.com
Equitherm	http://www.equitherm.com
Flir Systems	http://www.flir.com
Infrared Solutions	http://www.infraredsolutions.com
Indigo Systems	http://www.indigosystems.com
Land Infrared	http://www.landinst.com
Meditherm	http://www.meditherm.com
Raytheon	http://www.raytheoninfrared.com
Sierra Pacific Infrared	http://www.x20.org
Snell Infrared	http://www.snellinfrared.com
Teletherm	http://home1.gte.net/infrared
Vetel Diagnostics	http://www.veteldiagnostics.com

factors is the spectral range. For medical use the range of 8 to 14 μm is ideal because this is the peak emissivity of skin. From a practical standpoint there is also less environmental artifact at this range. This author prefers real-time thermography to still thermography because real-time eliminates any problems with motion, makes the examination more dynamic, and allows for faster imaging. *Sensitivity* refers to the amount of temperature difference that can be detected. Cooled units can differentiate within 0.01°C, whereas most uncooled units can differentiate within 0.1°C. Although a cooled unit is more sensitive, it has not been applicable to medical thermograms because 0.3°C is necessary for sensitivity. The final factor is portability and durability. In equine medicine an instrument needs to withstand the rigors of daily use and it must be easy to carry. Portable cooled units are usually expensive and fragile, whereas uncooled cameras that use the focal array technology are very portable and durable because they have no moving parts (Table 10.3-1)

THE PHYSIOLOGY OF THERMOGRAPHY

Heat is perpetually generated by the body and dissipated through the skin by radiation, convection, conduction, or evaporation. Because of this, skin temperature is generally 5°C (9°F) cooler than body core temperature (37°C). Skin derives its heat from the local circulation and tissue metabolism. Because tissue metabolism is generally constant, variation in skin temperature is usually caused by changes in local tissue perfusion. Veins are normally warmer than arteries because they drain metabolically active areas. Superficial veins will heat the skin more than superficial arteries, and venous drainage from tissues or organs with a high metabolic rate will be warmer than venous drainage from other tissues.

The circulatory pattern and the relative blood flow dictate the thermal pattern, which is the basis for thermographic interpretation. The normal thermal pattern of any area can be predicted on the basis of its vascularity and surface contour. Skin that covers muscle is also subject to temperature increase during muscle activity. On the basis

of these findings, some generalizations can be made regarding the thermal patterns of a horse: the midline will generally be warmer than other areas of the body. These areas include the back, the chest, between the rear legs, and along the ventral midline. Heat over the legs tends to follow the routes of the major vessels (i.e., the cephalic vein in front and the saphenous vein in the rear).

On the dorsal view of the distal limb, the metacarpus (metatarsus), fetlock, and pastern areas appear relatively cool compared to the rest of the body because the image recorded is away from the major blood supply. Thermographically, the warmest area in the distal limb is around the rich arteriovenous plexus of the coronary band and laminar corium located proximally on the hoof wall. There is normally increased warmth between the third metacarpus and flexor tendons, following the route of the median palmar vein in the foreleg and the metatarsal vein in the rear leg. Over the foot, the warmest area corresponds to the coronary band. From the palmar (plantar) aspect, the tendons are relatively cool and the warmest area is consistently between the bulbs of the heel along the midline.

Injured or diseased tissues will invariably have an altered circulation. One of the cardinal signs of inflammation is heat, which is caused by increased circulation. Thermographically, the "hot spot" associated with the localized inflammation will usually be seen in the skin that directly overlies the injury. However, diseased tissues may in fact have a reduced blood supply either because of swelling, thrombosis of vessels, or infarction of tissues. With such lesions the area of decreased heat is usually surrounded by increased thermal emissions, probably the result of shunting of blood.

PRODUCTION OF RELIABLE THERMOGRAMS

To produce reliable thermographic images the following factors need to be controlled: motion, artifacts, ambient temperature, and extraneous radiant energy. To control motion the clinician can immobilize the horse in stocks or use a qualified handler; however, the use of real-time thermography decreases the need for complete immobilization. Chemical restraining agents should be avoided because these drugs affect the peripheral circulation and cardiovascular system and could cause false thermal patterns to be produced. (This author has not encountered this problem, however.) To reduce the effects of extraneous radiant energy, thermography should be performed under cover shielded from the sun. Preferably, thermography should be done in darkness or low-level lighting. Ideally, ambient temperature should be in the range of 20°C (68°F) but any constant temperature, as long as the horse is not sweating, is acceptable. Heat loss from sweating does not occur below 30°C (86°F), because radiation and convection are responsible for heat loss below that temperature. Very cold environmental temperatures may cause vasoconstriction of the horse's lower legs and interfere with imaging. In these cases low-level exercise to stimulate vasodilatation is necessary. The thermographic area ideally should have a steady, uniform airflow so that erroneous cooling does not occur. For practical reasons, the horse should be kept from drafts and should be allowed 10 to 20 minutes to acclimate to the environment or room where thermography is performed.

Artifacts are extraneous sources on the skin that can cause irregular images. These sources include debris, scar tissue, hair length, liniments, leg wraps, and equipment. To avoid artifacts, all horses are groomed and free of leg wraps and equipment for 2 hours before scanning whenever possible. Hair insulates the leg and blocks the emission of infrared radiation. But as long as the hair is short and of uniform length, the thermal image produced should be accurate. The skin should always be evaluated for changes in hair length that may cause false “hot spots” in the thermogram.

Multiple thermographic images of a suspect area should be made. The area in question should be evaluated from at least two directions approximately 90 degrees apart to determine whether a “hot spot” is consistently present. The horse’s extremities should be examined from four directions (circumferentially). Significant areas of inflammation will appear over the same spot on each replicate thermogram.

USES OF THERMOGRAPHY

At least three uses exist for thermography in equine veterinary practice. The first is as a diagnostic tool. In these cases, thermography is a physiologic imaging method in which a 1° C difference between two anatomically symmetrical regions indicates a region of inflammation. In these cases, a decrease in temperature is as important as an increase in temperature. The image can be used to identify an area of interest to be pursued with an anatomic imaging method such as ultrasonography and/or radiography. The second method is to enhance the physical examination. In this case thermography is used to identify changes in heat and therefore locate “areas of suspicion.” Thermographic cameras are at least ten times more sensitive than the hand in determining temperature differences. This method is used to help identify asymmetry; the practitioner must then use the information to determine the actual cause and significance of the temperature difference. The third use of thermography is in a wellness program. In this method horses in training are followed weekly. In this author’s experience, thermographic changes often occur 2 weeks before clinical changes. In these cases thermography can be used to identify subclinical problems, and training alterations can then be made so that injury may be avoided altogether.

RELATIONSHIP OF THERMOGRAPHY TO OTHER IMAGING MODALITIES

With the continuous increase in technological capabilities for equine practice and improvements in imaging animals, the ability of veterinarians to make accurate diagnoses will continue to improve. It is important to understand that none of the newer imaging techniques can replace the physical examination. Rather, all imaging techniques only enhance the database established by the physical examination, and each imaging modality offers unique specific information. Similarly, each imaging modality correspondingly has its own limitations.

Thermography and scintigraphy are physiologic imaging modalities. They provide information about tissue physiology, especially circulation. They provide information as to the location of injury or disease as well as viability of the tissue. But neither provides information as to the specific nature of the problem. For this an anatomic

imaging modality can be used to identify the structure of the tissues in question.

Radiography is used to evaluate tissue contrasts, in particular changes in bone. Identification of these changes is used to determine injuries to bone. Unfortunately, excepting fractures, most radiographic changes in bone often take 10 to 14 days to become evident. Further, many of the bone changes are often permanent, so it can be difficult to determine whether a change, especially a chronic change, is the cause of pain and lameness. Thermography essentially images inflammation, which usually implies pain. In this respect, thermography can help to determine whether a radiographic change is associated with inflammation and therefore the possible cause of lameness.

Thermography and ultrasonography are complementary. Whereas thermography may be used to locate an injury, ultrasonography can be used to evaluate the injured structure’s morphology and the size and shape of the injury. Ultrasonography can be used to follow healing, but thermography can be used to evaluate “when” the inflammatory process is resolved.

Scintigraphy has been most useful for the detection of radiographically occult skeletal lesions. Thermography complements this technique because scintigraphy can selectively be used to evaluate bone and thermography specifically to evaluate the overlying soft tissues.

CONCLUSIONS

Thermography—the pictorial representation of skin temperature that involves the detection of infrared radiation, which can be correlated directly to blood flow—is a practical aid in the clinical evaluation of the equine patient. This modality is particularly germane to the evaluation of lameness and can be used to specifically increase the accuracy of diagnosis. To be accurate, thermography must be performed in a controlled area free of drafts that should be protected from sunlight to avoid erroneous heating of the skin, and the hair length should be uniform. Thermography can be used to detect heat before it is perceptible during routine physical examination and therefore is useful for early detection of laminitis, stress fractures, and tendinitis. Thermography offers a noninvasive means of evaluating the blood supply to an injured region and offers one of the only reliable noninvasive means to evaluate blood flow to the foot of the horse. This method is also useful for the early identification of stress injuries to the contralateral limb of convalescing orthopedic patients. Thermography is an excellent adjunct to clinical examination and a complement to other imaging techniques such as radiology, ultrasonography, and scintigraphy.

Supplemental Readings

- Graf von Schweinitz D: Thermographic diagnostics in equine back pain. *Vet Clin North Am Equine Pract* 1999;15:161-177.
- Turner TA: Diagnostic thermography. *Vet Clin North Am Equine Pract* 2001; 17:95-113.
- Turner TA, Pansch J, Wilson JH: Thermographic assessment of racing thoroughbreds. *Proceedings of the 47th Annual Meeting of the American Association of Equine Practitioners*, pp 344-346, 2001.

CHAPTER 10.4

Clinical Uses of Computed Tomography

CHRISTOPHER E. KAWCAK

Fort Collins, Colorado

ELWYN FIRTH

Palmerston North, New Zealand

DOUG J. HERTHEL

Los Olivos, California

EMILY A. SANDLER

Santa Ynez, California

Computed tomography (CT) has become a common imaging modality available at referral equine hospitals across the world; however, only recently have the true indications for use of CT become apparent. During CT, cross-sectional radiographic images are created within a circular gantry by the generation of x-rays from a rotating x-ray tube. The x-ray images then are received by a number of radiation detector cells opposite the beam. Each detector generates a CT number (Hounsfield unit) that is indicative of the radiation received after attenuation by the tissues. Water represents a Hounsfield number of zero, and bone is usually represented by a Hounsfield number of approximately 1000. The ability to detect lesions is the result of different Hounsfield numbers of normal and pathologic bone that can be used to detect a 0.5% change in density, as opposed to the 10% change in density needed to see change with radiography. A series of two-dimensional transverse images are generated that can be reconstructed in other planes; these images also can be rendered into three-dimensional images that can be used to assess lesions or density patterns or can be used for surgical planning. This chapter describes machines that are currently in use at several referral hospitals and details the indications for use of these machines.

SCANNERS

Various types of scanners are now in use both in veterinary and human hospitals. Most veterinary CT units are single slice units; however, multislice units are now available that can take multiple planes, which decreases the scanning time. Spiral scanners are also available that have been used for "real-time" scanning for cardiac patients. Peripheral quantitative CT scanners (pQCT) are low-radiation, table-top units that have been used to measure bone density in humans for several years.

All veterinary CT scanning currently requires the animal to be anesthetized. The configuration of CT machines makes it unlikely that a standing CT unit will be created in the near future. Therefore, the greatest obstacle to those ob-

taining CT images from horses has been the lack of a reliable table on which the horse can lie to allow precise movement of the animal into the gantry. However, two methods have been used for horses. The stationary unit/movable table model (Luminys Table, Universal Medical Systems, Salton, Ohio) uses a custom-designed table which is moved by the CT couch at precise increments. The anesthetized horse is hoisted onto the table and secured.

The stationary table/movable unit model (Philips Tomoscan M, Philips Medical Systems, Best, Netherlands) has been used in private practice for several years with good success. The animal is placed onto a surgery table and the CT unit is placed over the animal and locked to the table. The CT gantry then moves at precise increments over the area of interest for imaging.

The pQCT works in a similar way in that the gantry moves over the horse's area of interest (XCT2000, Stratec, Pforzheim, Germany). Its limitation is that the gantry is only large enough for the distal aspect of a horse's limb (Figure 10.4-1), although other models have a 300-mm gantry.



Figure 10.4-1 Imaging of a foal carpus in a peripheral quantitative computed tomography (pQCT) machine. The limb is kept straight within the gantry, which moves over the region of interest. Therefore no movement of the animal is necessary.

CLINICAL INDICATIONS

CT imaging has been performed mostly on distal extremities and the skull and cranial cervical areas. The regions of a full-sized horse that can be imaged include the entire head and upper neck to the second or third cervical vertebrae area. Additionally, the front legs up to the carpus and the hind legs including the hock and distal tibia can also be imaged. In horses weighing less than 1000 pounds the stifle area can also be imaged. The entire body, including thorax, abdomen and pelvis, can be scanned in foals and Miniature Horses that weigh less than 400 pounds.

In the distal extremities, CT imaging has been used to diagnose joint-related diseases that have been radiographically silent or that required enhanced visualization for diagnosis or enhanced imaging for better preoperative planning. This method is best used to assess subchondral sclerosis, and enostosis; however, although CT can be very reliable for assessing enthesiophytes and osteophytes, sometimes a phenomenon known as “volume averaging” can allow these lesions to be missed. Volume averaging occurs when a voxel, or three-dimensional space that is imaged, has both bone and soft tissue present. The density will be read as falsely low, leading to an area of bone that is not imaged. Consequently, small lesions such as enthesiophytes and osteophytes could be missed or even falsely interpreted as areas of marginal lysis. In these cases, the CT results should be compared with high-detail radiographs for proper diagnosis. CT has also been helpful for the diagnosis of lytic lesions surrounded by sclerosis, in which radiographs usually are normal (Figure 10.4-2).

Digit

CT imaging has been used to visualize radiographically silent lesions of the digital area. Specifically, extensive solar margin lesions that were not seen on radiographs because of superimposition of associated structures have been readily visible with CT. Furthermore, cystic lesions in the coffin bone have been imaged and rendered into three dimensions to determine the best surgical route needed for debridement. Areas of soft tissue mineralization have also been seen, including adhesions and calcification of the attachment of the deep digital flexor tendon into the third phalanx (P3).

Fetlock

Various lesions in the fetlock joints have been visualized with CT. Specifically, cystic lesions in the first phalanx, both septic and aseptic, have been visualized. These images have allowed for presurgical planning and better assessment of involvement compared with radiographs. Palmar/plantar third metacarpal/metatarsal lesions have also been better visualized by using CT compared with radiographs. Lesions in the proximal sesamoid bones have also been seen in joints that were radiographically normal. Not only has CT allowed for better presurgical planning compared with radiographs, but they have also given clinicians a better means of early diagnosis and better postoperative assessment.

Metacarpal Region

pQCT has been used to help diagnose aberrant bone reaction to exercise. For instance, pQCT has been used by one of this chapter's authors (EF) to rule out second metacarpal bone fracture, and in doing so, demonstrated that deposition of low density bone was present. This finding led to the recommendation of continued rest until bone remodeling was complete, which occurred several months later (Figure 10.4-3). This case further demonstrates the usefulness of CT in the diagnosis of subtle changes in bone character.

Carpus

Various lesions have been detected in the carpal joints of horses. Specifically, one of the authors (DH) of this chapter has used CT to diagnose a cyst in the ulnar carpal bone of a horse. This method provided excellent preoperative assessment and a good means of following up healing. Third carpal bone disease, also known as *stress-induced disease*, has also been more closely diagnosed and monitored with CT than with radiographs. Specifically, third carpal bone sclerosis and a combination of sclerosis and centralized lysis have been seen in some of these horses. Detection of sclerosis is beneficial in that it may signify changes in an area that could lead to catastrophic injury. One area in which CT is deficient in the carpus is diagnosis of intercarpal ligament injuries. Unless there is an area of sclerosis around the insertion of the ligaments on the carpal bones, these lesions can be missed.



Figure 10.4-2 A transverse computed tomography (CT) slice through the distal third metacarpal region of a horse showing a cystic lesion (C) with surrounding sclerosis. The cystic lesion could not be discerned radiographically, possibly because of the intense sclerosis around the area that may have superimposed over the cyst.

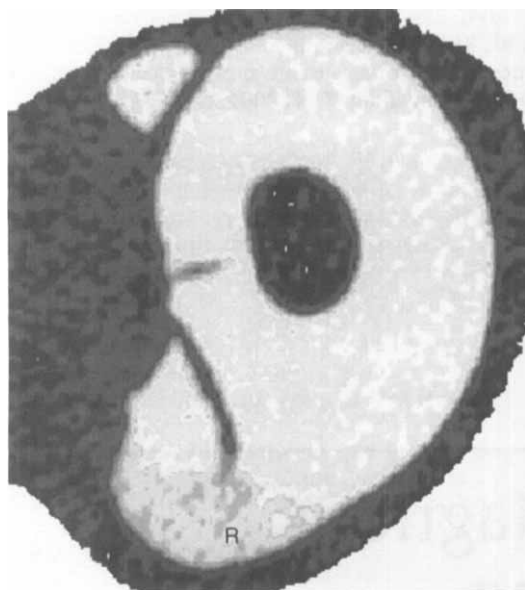


Figure 10.4-3 A transverse computed tomography (CT) image of the metacarpal area obtained with a peripheral quantitative CT (pQCT) machine. Note the area of bone reaction (*R*) and fusion between the third and second metacarpal bones. Color enhancement of the image showed the reactive bone to be of low density.

Tarsus

Cysts of the distal tibia, talus lysis, subtle fractures, and medial malleolus lysis in horses have been diagnosed with CT and reported. Some of these lesions were septic, and CT allowed for visualization of the septic nidus, which helped to resolve septic arthritis after localization and debridement.

Head

CT imaging has been a valuable tool to characterize diseases of the face and head. For instance, in a group of horses with nasal discharge and minimal radiographic changes, one group found that most of the horses had some degree of maxillary fluid accumulation, occasional ethmoid masses, mucosal and bone thickening, and alveolus elevation around the fourth premolar and first molar teeth. Other more rare lesions, such as brain tumors, calvaria fractures, stylohyoid fractures and callus, periorbital lesions, dental origin cysts, and lesions in the inner and middle ear have also been seen by using CT. Invasive lesions in the nasal and sinus areas have also been recognized and surgical margins determined from those images (Figure 10.4-4). Contrast enhancement of brain lesions with CT has also been performed to enhance visualization. One of the greatest benefits of CT appears to be the ability to image distinct structures in the head area.

Spine

Cranial cervical lesions can also be imaged in most machines. Diseases such as facet arthritis and traumatic lesions can often be seen clearly with CT.

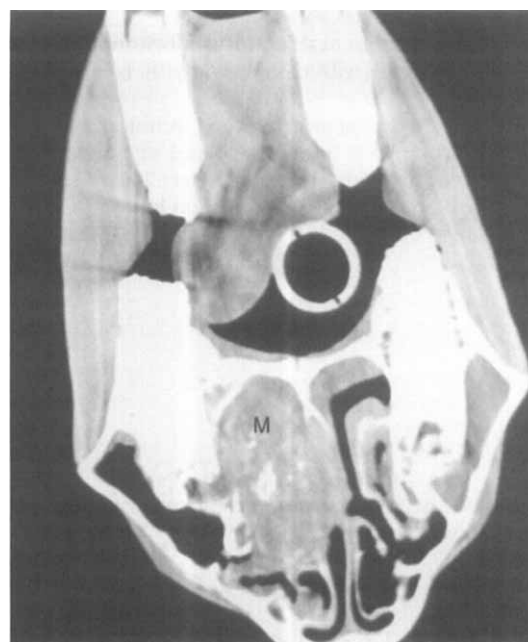


Figure 10.4-4 A transverse computed tomography (CT) image of a skull showing a large sinus mass (*M*). The image allowed for presurgical planning in this case.

BONE DENSITY

Because CT images are produced from an indirect measure of density and classified according to a relative measure of density (Hounsfield unit), an objective measure of cortical and subchondral density can be achieved by scanning patients with the inclusion of a density phantom. The phantom contains material of various densities that can be imaged, measured in Hounsfield units, and used as a standard to calculate density in bone. Density can be calculated on slices by using either conventional CT or pQCT. Three-dimensional images have also been rendered and density “maps” created to determine the loading of a horse’s joint.

In summary, the use of CT in equine practice is still limited to a few referral hospitals; however, indications for its use are becoming clearer. The use of this imaging modality is not taken lightly because of the need for general anesthesia, yet those practitioners who use this modality are excellent references for clinicians seeking to determine the appropriateness of CT imaging for particular cases.

Supplemental Readings

- Barbee DD, Allen JR, Grant BD: Detection by computed tomography of occult osteochondral defects in the fetlock of a horse. *Equine Vet J* 1987; 19:556-558.
- Firth EC, Rogers CW, Faram T: pQCT assessment of some distal limb bone characteristics in pasture-raised New Zealand thoroughbred horses up to 410 days of age. *Equine Vet J* (in press).

Hanson JA, Seeherman HJ, Kirker-Head CA et al: The role of computed tomography in evaluation of subchondral osseous lesions in seven horses with chronic synovitis. *Equine Vet J* 1996; 28:480-488.

Kraft SL, Gavin P: Physical principles and technical considerations for equine computed tomography and magnetic resonance imaging. *Vet Clin North Am Equine Pract* 2001; 17:115-130.

Martens P, Asbjörn T, Jon T: Identification by computed tomography of a radiographically occult lesion in the distal phalanx of a Standardbred horse. *Equine Practice* 2000; 22:12-15.

Tucker RL, Farrell E: Computed tomography and magnetic resonance imaging of the equine head. *Vet Clin North Am Equine Pract* 2001; 17:131-144.

Tucker RL, Sande RD: Computed tomography and magnetic resonance imaging of the equine musculoskeletal conditions. *Vet Clin North Am Equine Pract* 2001; 17:145-147.

CHAPTER 10.5

Clinical Uses of Magnetic Resonance Imaging

RUSSELL L. TUCKER
Pullman, Washington

Magnetic resonance imaging (MRI) is now available for imaging equine patients at a few veterinary institutions. MRI provides images with unparalleled tissue contrast and anatomic definition and offers several diagnostic advantages over other imaging technologies. In particular, the ability of MRI to demonstrate physiologic and anatomic information can be a great benefit in the early diagnosis of many orthopedic conditions. Consequently, the use of MRI in certain equine patients should allow for more timely intervention and therefore improve the prognosis and long-term outcome.

MRI is accomplished by using the magnetic properties of tissues. With MRI the legs of the horse first must be positioned within the center of a strong external magnetic field generated by the MRI system (Figure 10.5-1, A). Free protons (primarily hydrogen protons) within tissues, acting as small magnetic dipoles, are subjected to repetitive, perturbing radiofrequency pulses. Under the influence of the perturbing radiofrequency pulses, the free protons briefly are knocked out of magnetic alignment. Once the perturbing radiofrequency pulse is discontinued, the free protons return to alignment relative to the external magnetic field. As the free protons realign themselves, they emit a radiofrequency signal, which is collected to create the image. For most equine orthopedic applications, a receiving coil is placed closely around the anatomic region of interest to collect the emitted signal (Figure 10.5-1, B).

MRI displays anatomic and physiologic detail in both the osseous and soft tissue structures. Similar to ultrasonography and computed tomography, MRI yields images as tomographic slices. The MRI operator determines the thickness and orientation of the slices. MRI of equine or-

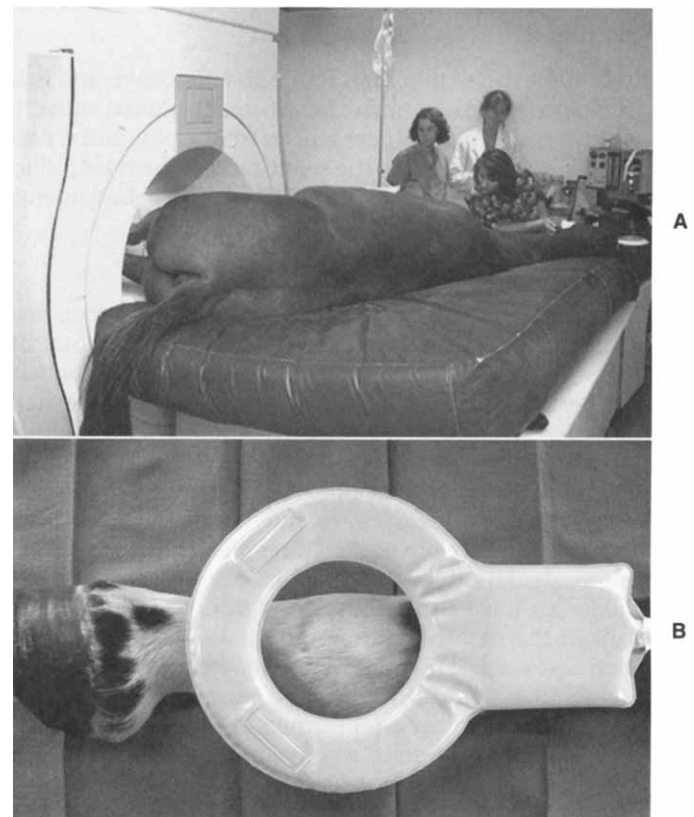


Figure 10.5-1 **A**, Adult horse positioned in the magnetic resonance imaging (MRI) unit for imaging of the rear legs. Both rear legs simultaneously are placed into the center of the imaging gantry. **B**, Photograph of a circular receiving coil fitted over the fetlock joint.

CHAPTER 10.4

Clinical Uses of Computed Tomography

CHRISTOPHER E. KAWCAK

Fort Collins, Colorado

ELWYN FIRTH

Palmerston North, New Zealand

DOUG J. HERTHEL

Los Olivos, California

EMILY A. SANDLER

Santa Ynez, California

Computed tomography (CT) has become a common imaging modality available at referral equine hospitals across the world; however, only recently have the true indications for use of CT become apparent. During CT, cross-sectional radiographic images are created within a circular gantry by the generation of x-rays from a rotating x-ray tube. The x-ray images then are received by a number of radiation detector cells opposite the beam. Each detector generates a CT number (Hounsfield unit) that is indicative of the radiation received after attenuation by the tissues. Water represents a Hounsfield number of zero, and bone is usually represented by a Hounsfield number of approximately 1000. The ability to detect lesions is the result of different Hounsfield numbers of normal and pathologic bone that can be used to detect a 0.5% change in density, as opposed to the 10% change in density needed to see change with radiography. A series of two-dimensional transverse images are generated that can be reconstructed in other planes; these images also can be rendered into three-dimensional images that can be used to assess lesions or density patterns or can be used for surgical planning. This chapter describes machines that are currently in use at several referral hospitals and details the indications for use of these machines.

SCANNERS

Various types of scanners are now in use both in veterinary and human hospitals. Most veterinary CT units are single slice units; however, multislice units are now available that can take multiple planes, which decreases the scanning time. Spiral scanners are also available that have been used for "real-time" scanning for cardiac patients. Peripheral quantitative CT scanners (pQCT) are low-radiation, table-top units that have been used to measure bone density in humans for several years.

All veterinary CT scanning currently requires the animal to be anesthetized. The configuration of CT machines makes it unlikely that a standing CT unit will be created in the near future. Therefore, the greatest obstacle to those ob-

taining CT images from horses has been the lack of a reliable table on which the horse can lie to allow precise movement of the animal into the gantry. However, two methods have been used for horses. The stationary unit/movable table model (Luminys Table, Universal Medical Systems, Salton, Ohio) uses a custom-designed table which is moved by the CT couch at precise increments. The anesthetized horse is hoisted onto the table and secured.

The stationary table/movable unit model (Philips Tomoscan M, Philips Medical Systems, Best, Netherlands) has been used in private practice for several years with good success. The animal is placed onto a surgery table and the CT unit is placed over the animal and locked to the table. The CT gantry then moves at precise increments over the area of interest for imaging.

The pQCT works in a similar way in that the gantry moves over the horse's area of interest (XCT2000, Stratec, Pforzheim, Germany). Its limitation is that the gantry is only large enough for the distal aspect of a horse's limb (Figure 10.4-1), although other models have a 300-mm gantry.



Figure 10.4-1 Imaging of a foal carpus in a peripheral quantitative computed tomography (pQCT) machine. The limb is kept straight within the gantry, which moves over the region of interest. Therefore no movement of the animal is necessary.

CLINICAL INDICATIONS

CT imaging has been performed mostly on distal extremities and the skull and cranial cervical areas. The regions of a full-sized horse that can be imaged include the entire head and upper neck to the second or third cervical vertebrae area. Additionally, the front legs up to the carpus and the hind legs including the hock and distal tibia can also be imaged. In horses weighing less than 1000 pounds the stifle area can also be imaged. The entire body, including thorax, abdomen and pelvis, can be scanned in foals and Miniature Horses that weigh less than 400 pounds.

In the distal extremities, CT imaging has been used to diagnose joint-related diseases that have been radiographically silent or that required enhanced visualization for diagnosis or enhanced imaging for better preoperative planning. This method is best used to assess subchondral sclerosis, and enostosis; however, although CT can be very reliable for assessing enthesiophytes and osteophytes, sometimes a phenomenon known as “volume averaging” can allow these lesions to be missed. Volume averaging occurs when a voxel, or three-dimensional space that is imaged, has both bone and soft tissue present. The density will be read as falsely low, leading to an area of bone that is not imaged. Consequently, small lesions such as enthesiophytes and osteophytes could be missed or even falsely interpreted as areas of marginal lysis. In these cases, the CT results should be compared with high-detail radiographs for proper diagnosis. CT has also been helpful for the diagnosis of lytic lesions surrounded by sclerosis, in which radiographs usually are normal (Figure 10.4-2).

Digit

CT imaging has been used to visualize radiographically silent lesions of the digital area. Specifically, extensive solar margin lesions that were not seen on radiographs because of superimposition of associated structures have been readily visible with CT. Furthermore, cystic lesions in the coffin bone have been imaged and rendered into three dimensions to determine the best surgical route needed for debridement. Areas of soft tissue mineralization have also been seen, including adhesions and calcification of the attachment of the deep digital flexor tendon into the third phalanx (P3).

Fetlock

Various lesions in the fetlock joints have been visualized with CT. Specifically, cystic lesions in the first phalanx, both septic and aseptic, have been visualized. These images have allowed for presurgical planning and better assessment of involvement compared with radiographs. Palmar/plantar third metacarpal/metatarsal lesions have also been better visualized by using CT compared with radiographs. Lesions in the proximal sesamoid bones have also been seen in joints that were radiographically normal. Not only has CT allowed for better presurgical planning compared with radiographs, but they have also given clinicians a better means of early diagnosis and better postoperative assessment.

Metacarpal Region

pQCT has been used to help diagnose aberrant bone reaction to exercise. For instance, pQCT has been used by one of this chapter's authors (EF) to rule out second metacarpal bone fracture, and in doing so, demonstrated that deposition of low density bone was present. This finding led to the recommendation of continued rest until bone remodeling was complete, which occurred several months later (Figure 10.4-3). This case further demonstrates the usefulness of CT in the diagnosis of subtle changes in bone character.

Carpus

Various lesions have been detected in the carpal joints of horses. Specifically, one of the authors (DH) of this chapter has used CT to diagnose a cyst in the ulnar carpal bone of a horse. This method provided excellent preoperative assessment and a good means of following up healing. Third carpal bone disease, also known as *stress-induced disease*, has also been more closely diagnosed and monitored with CT than with radiographs. Specifically, third carpal bone sclerosis and a combination of sclerosis and centralized lysis have been seen in some of these horses. Detection of sclerosis is beneficial in that it may signify changes in an area that could lead to catastrophic injury. One area in which CT is deficient in the carpus is diagnosis of intercarpal ligament injuries. Unless there is an area of sclerosis around the insertion of the ligaments on the carpal bones, these lesions can be missed.



Figure 10.4-2 A transverse computed tomography (CT) slice through the distal third metacarpal region of a horse showing a cystic lesion (C) with surrounding sclerosis. The cystic lesion could not be discerned radiographically, possibly because of the intense sclerosis around the area that may have superimposed over the cyst.

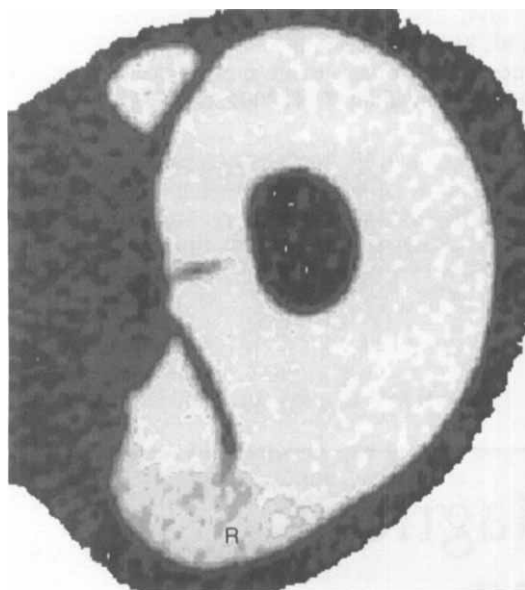


Figure 10.4-3 A transverse computed tomography (CT) image of the metacarpal area obtained with a peripheral quantitative CT (pQCT) machine. Note the area of bone reaction (*R*) and fusion between the third and second metacarpal bones. Color enhancement of the image showed the reactive bone to be of low density.

Tarsus

Cysts of the distal tibia, talus lysis, subtle fractures, and medial malleolus lysis in horses have been diagnosed with CT and reported. Some of these lesions were septic, and CT allowed for visualization of the septic nidus, which helped to resolve septic arthritis after localization and debridement.

Head

CT imaging has been a valuable tool to characterize diseases of the face and head. For instance, in a group of horses with nasal discharge and minimal radiographic changes, one group found that most of the horses had some degree of maxillary fluid accumulation, occasional ethmoid masses, mucosal and bone thickening, and alveolus elevation around the fourth premolar and first molar teeth. Other more rare lesions, such as brain tumors, calvaria fractures, stylohyoid fractures and callus, periorbital lesions, dental origin cysts, and lesions in the inner and middle ear have also been seen by using CT. Invasive lesions in the nasal and sinus areas have also been recognized and surgical margins determined from those images (Figure 10.4-4). Contrast enhancement of brain lesions with CT has also been performed to enhance visualization. One of the greatest benefits of CT appears to be the ability to image distinct structures in the head area.

Spine

Cranial cervical lesions can also be imaged in most machines. Diseases such as facet arthritis and traumatic lesions can often be seen clearly with CT.

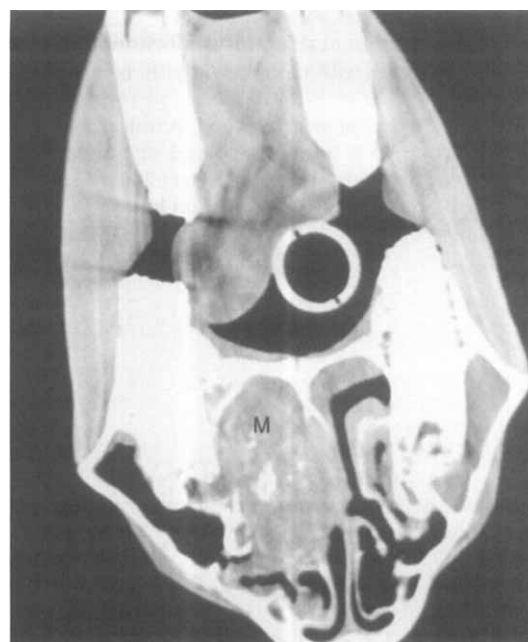


Figure 10.4-4 A transverse computed tomography (CT) image of a skull showing a large sinus mass (*M*). The image allowed for presurgical planning in this case.

BONE DENSITY

Because CT images are produced from an indirect measure of density and classified according to a relative measure of density (Hounsfield unit), an objective measure of cortical and subchondral density can be achieved by scanning patients with the inclusion of a density phantom. The phantom contains material of various densities that can be imaged, measured in Hounsfield units, and used as a standard to calculate density in bone. Density can be calculated on slices by using either conventional CT or pQCT. Three-dimensional images have also been rendered and density "maps" created to determine the loading of a horse's joint.

In summary, the use of CT in equine practice is still limited to a few referral hospitals; however, indications for its use are becoming clearer. The use of this imaging modality is not taken lightly because of the need for general anesthesia, yet those practitioners who use this modality are excellent references for clinicians seeking to determine the appropriateness of CT imaging for particular cases.

Supplemental Readings

- Barbee DD, Allen JR, Grant BD: Detection by computed tomography of occult osteochondral defects in the fetlock of a horse. *Equine Vet J* 1987; 19:556-558.
- Firth EC, Rogers CW, Faram T: pQCT assessment of some distal limb bone characteristics in pasture-raised New Zealand thoroughbred horses up to 410 days of age. *Equine Vet J* (in press).

Hanson JA, Seeherman HJ, Kirker-Head CA et al: The role of computed tomography in evaluation of subchondral osseous lesions in seven horses with chronic synovitis. *Equine Vet J* 1996; 28:480-488.

Kraft SL, Gavin P: Physical principles and technical considerations for equine computed tomography and magnetic resonance imaging. *Vet Clin North Am Equine Pract* 2001; 17:115-130.

Martens P, Asbjörn T, Jon T: Identification by computed tomography of a radiographically occult lesion in the distal phalanx of a Standardbred horse. *Equine Practice* 2000; 22:12-15.

Tucker RL, Farrell E: Computed tomography and magnetic resonance imaging of the equine head. *Vet Clin North Am Equine Pract* 2001; 17:131-144.

Tucker RL, Sande RD: Computed tomography and magnetic resonance imaging of the equine musculoskeletal conditions. *Vet Clin North Am Equine Pract* 2001; 17:145-147.

CHAPTER 10.5

Clinical Uses of Magnetic Resonance Imaging

RUSSELL L. TUCKER
Pullman, Washington

Magnetic resonance imaging (MRI) is now available for imaging equine patients at a few veterinary institutions. MRI provides images with unparalleled tissue contrast and anatomic definition and offers several diagnostic advantages over other imaging technologies. In particular, the ability of MRI to demonstrate physiologic and anatomic information can be a great benefit in the early diagnosis of many orthopedic conditions. Consequently, the use of MRI in certain equine patients should allow for more timely intervention and therefore improve the prognosis and long-term outcome.

MRI is accomplished by using the magnetic properties of tissues. With MRI the legs of the horse first must be positioned within the center of a strong external magnetic field generated by the MRI system (Figure 10.5-1, A). Free protons (primarily hydrogen protons) within tissues, acting as small magnetic dipoles, are subjected to repetitive, perturbing radiofrequency pulses. Under the influence of the perturbing radiofrequency pulses, the free protons briefly are knocked out of magnetic alignment. Once the perturbing radiofrequency pulse is discontinued, the free protons return to alignment relative to the external magnetic field. As the free protons realign themselves, they emit a radiofrequency signal, which is collected to create the image. For most equine orthopedic applications, a receiving coil is placed closely around the anatomic region of interest to collect the emitted signal (Figure 10.5-1, B).

MRI displays anatomic and physiologic detail in both the osseous and soft tissue structures. Similar to ultrasonography and computed tomography, MRI yields images as tomographic slices. The MRI operator determines the thickness and orientation of the slices. MRI of equine or-

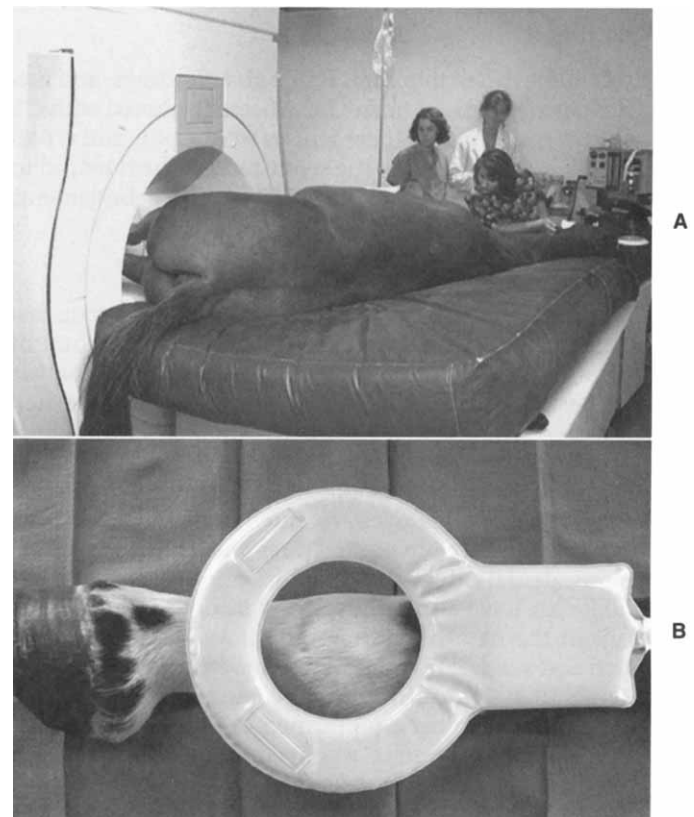


Figure 10.5-1 **A**, Adult horse positioned in the magnetic resonance imaging (MRI) unit for imaging of the rear legs. Both rear legs simultaneously are placed into the center of the imaging gantry. **B**, Photograph of a circular receiving coil fitted over the fetlock joint.

Hanson JA, Seeherman HJ, Kirker-Head CA et al: The role of computed tomography in evaluation of subchondral osseous lesions in seven horses with chronic synovitis. *Equine Vet J* 1996; 28:480-488.

Kraft SL, Gavin P: Physical principles and technical considerations for equine computed tomography and magnetic resonance imaging. *Vet Clin North Am Equine Pract* 2001; 17:115-130.

Martens P, Asbjörn T, Jon T: Identification by computed tomography of a radiographically occult lesion in the distal phalanx of a Standardbred horse. *Equine Practice* 2000; 22:12-15.

Tucker RL, Farrell E: Computed tomography and magnetic resonance imaging of the equine head. *Vet Clin North Am Equine Pract* 2001; 17:131-144.

Tucker RL, Sande RD: Computed tomography and magnetic resonance imaging of the equine musculoskeletal conditions. *Vet Clin North Am Equine Pract* 2001; 17:145-147.

CHAPTER 10.5

Clinical Uses of Magnetic Resonance Imaging

RUSSELL L. TUCKER
Pullman, Washington

Magnetic resonance imaging (MRI) is now available for imaging equine patients at a few veterinary institutions. MRI provides images with unparalleled tissue contrast and anatomic definition and offers several diagnostic advantages over other imaging technologies. In particular, the ability of MRI to demonstrate physiologic and anatomic information can be a great benefit in the early diagnosis of many orthopedic conditions. Consequently, the use of MRI in certain equine patients should allow for more timely intervention and therefore improve the prognosis and long-term outcome.

MRI is accomplished by using the magnetic properties of tissues. With MRI the legs of the horse first must be positioned within the center of a strong external magnetic field generated by the MRI system (Figure 10.5-1, A). Free protons (primarily hydrogen protons) within tissues, acting as small magnetic dipoles, are subjected to repetitive, perturbing radiofrequency pulses. Under the influence of the perturbing radiofrequency pulses, the free protons briefly are knocked out of magnetic alignment. Once the perturbing radiofrequency pulse is discontinued, the free protons return to alignment relative to the external magnetic field. As the free protons realign themselves, they emit a radiofrequency signal, which is collected to create the image. For most equine orthopedic applications, a receiving coil is placed closely around the anatomic region of interest to collect the emitted signal (Figure 10.5-1, B).

MRI displays anatomic and physiologic detail in both the osseous and soft tissue structures. Similar to ultrasonography and computed tomography, MRI yields images as tomographic slices. The MRI operator determines the thickness and orientation of the slices. MRI of equine or-

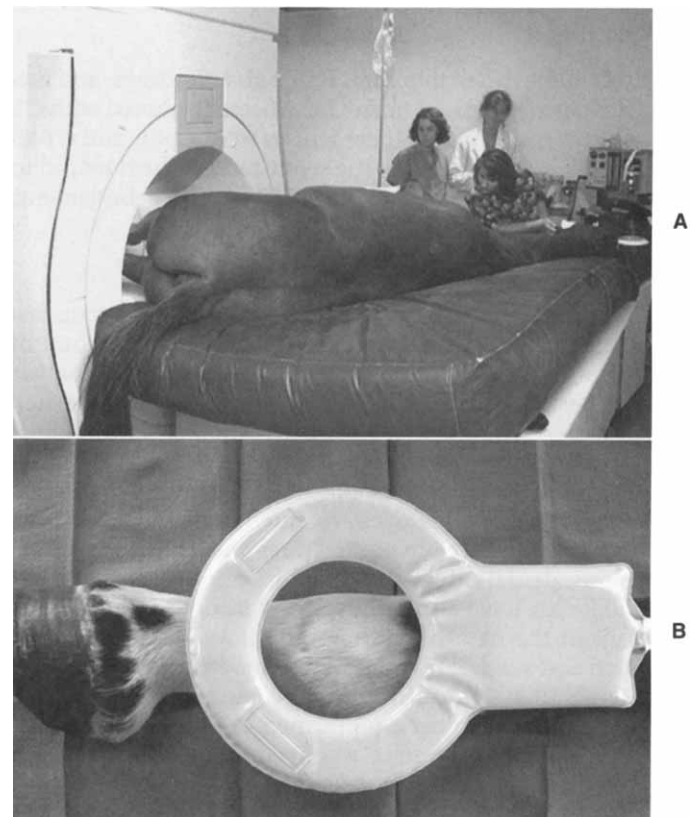


Figure 10.5-1 **A**, Adult horse positioned in the magnetic resonance imaging (MRI) unit for imaging of the rear legs. Both rear legs simultaneously are placed into the center of the imaging gantry. **B**, Photograph of a circular receiving coil fitted over the fetlock joint.

thopedic cases is commonly acquired in two to three orthogonal image planes. In some cases, additional image planes are selected to better evaluate specific structures and more precisely define relative anatomy. Similar to other digital imaging modalities, alternative MRI planes may be constructed in two-dimensional (2-D) and three-dimensional (3-D) images.

MAGNETIC RESONANCE IMAGING SEQUENCES FOR ORTHOPEDIC DISEASE

MRI of orthopedic disease is performed routinely in several different acquisition sequences. Each sequence displays slightly different anatomic, physiologic, and pathologic information. A common MRI protocol, known as *spin-echo imaging*, includes three types of acquisition sequences: T1-weighted (T1-wt), proton density (PD), and T2-weighted (T2-wt) images. All or some combination of sequences usually is acquired in each anatomic plane as each sequence provides different diagnostic information. The T1-wt images highlight the structural characteristics of tissues and are useful in evaluating the anatomy of bone and some soft tissues. T1-wt sequences also are used for the visualization of MRI paramagnetic contrast agents. Proton density images offer excellent tissue contrast and are used for evaluating both osseous and soft tissue structures. T2-wt images emphasize the fluid characteristics of tissues and are sensitive for detecting synovial effusions, cystic lesions, and areas of inflammation or edema in orthopedic injuries.

In addition to spin-echo protocols, several additional imaging sequences are often useful in orthopedic imaging. Sequences that suppress the normal fat signal (fat-suppression or fat-saturation) allow for recognition of edema and inflammation, which are often masked by the normal high signal of fat. Fat-suppression images are particularly useful for identification of trabecular bone edema and inflammation associated with microfractures that occur in the early phases of many orthopedic diseases. Subchondral bone contusions and bruising are an important diagnostic feature of acute articular injuries that can go unrecognized unless a fat-suppression sequence is obtained. Other imaging protocols, such as gradient echo imaging, are useful when thin tomographic slices are desired.

With most spin-echo imaging, it is necessary to maintain the slice thickness between 3 and 10 mm and maintain a 10% gap between slices to achieve adequate signal-to-noise ratio and avoid crosstalk between slices. Gradient-echo imaging allows contiguous slices as thin as 1 to 2 mm. Gradient-echo imaging volume acquisitions are useful when complex and multiplanar reconstructions are desired. Other sequences, such as magnetic transfer contrast imaging, can enhance contrast between adjacent tissues such as the articular cartilage and synovial fluid within joints. Abnormal cartilage may be seen better in the presence of joint effusion, which improves the detection of cartilage fissures and fractures as well as osteochondral lesions. Recently, sequences such as spoiled gradient echo techniques have improved evaluation of articular cartilage. New sequences are currently under development and probably will lead to several useful protocols for equine patients.

MAGNETIC RESONANCE IMAGING APPLICATIONS IN ORTHOPEDIC DISEASE

The applications of MRI in equine orthopedic disease have not yet been fully explored. MRI anatomy of the equine foot, navicular bone, fetlock, carpal, tarsal, and stifle joints have all been described. Most anatomic studies were accomplished post mortem using isolated limbs. The ability to image the distal legs of live adult horses, from the level of the carpal/tarsal joints to the distal foot, can be accomplished with minor accommodations in current MRI systems. Newer open-magnet design MRI systems should facilitate imaging of the proximal limbs and cervical region.

MRI has provided the diagnosis in many cases when other modalities failed to clearly identify the cause of lameness. This is especially true for soft tissue injuries around joints and in anatomic regions difficult to palpate or image by other methods. For example, the suspensory ligaments, the distal sesamoidean ligaments, and the flexor tendons are challenging to evaluate in their entirety from origin to insertion. MRI allows detection of lesions within the ligaments and tendons along their entire course (Figure 10.5-2). Furthermore, lesions associated with the distal sesamoidean ligaments can be difficult to diagnose because of the complex anatomy and limited access. MRI allows for clear visualization of all of the distal sesamoidean ligaments and is sensitive to soft tissue changes associated with ligament injuries. MRI provides high-resolution images of the anatomic alterations in addition to demonstration of internal integrity within the ligaments (Figure 10.5-3).

Several osseous injuries can be diagnosed with MRI before detection by other modalities. In particular, injuries that induce abnormal subchondral stress early in the disease process can be demonstrated readily. Bone edema and inflammation result in a focal increase in the fluid content. Fluid-sensitive MRI sequences allow illustration of these changes far in advance of radiographic detection. The early recognition of such lesions provides the opportunity to intervene and improves prognosis. This is especially true with articular injuries when early diagnosis and intervention may prevent further articular cartilage destruction (Figure 10.5-4).

MRI also has provided an imaging technique to allow recognition of initial onset of navicular degeneration. Early in the disease process, MRI can be used to detect inflammation of the synovial invaginations and within the medullary cavity of the navicular bone. In addition, the suspensory ligaments of the navicular, the navicular bursa, and the impar ligament can be evaluated using MRI. Importantly, MRI is capable of demonstrating cortical erosions along the flexor surface of the navicular bone and adhesions to the adjacent deep digital flexor tendon (Figure 10.5-5).

Arthrography is also possible using MRI. It can be helpful to expand the synovial volume of joints utilizing sterile saline injections to improve visualization of lesions. The disadvantage of this technique is the poor differentiation between the expanded synovial volume and the articular cartilage. Alternatively, paramagnetic contrast agents can be diluted and safely administered for arthrography. If needed, the paramagnetic contrast can be mixed with conventional radiographic contrast to allow for ra-

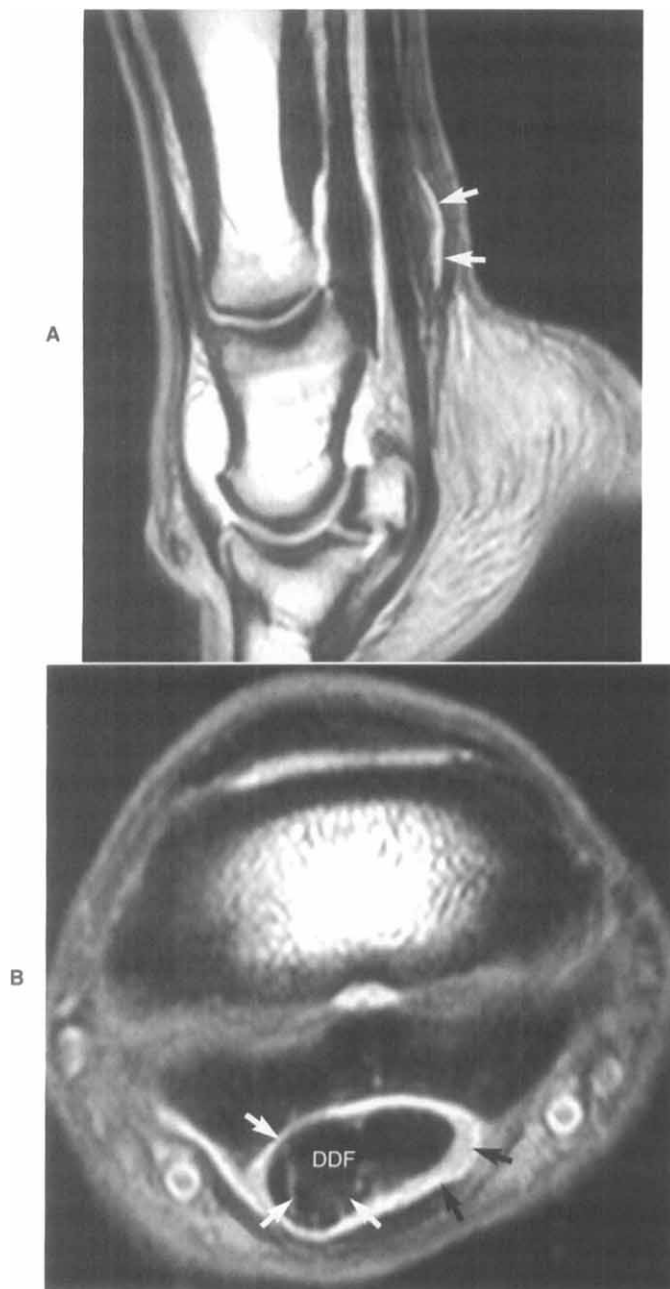


Figure 10.5-2 **A**, Proton density sagittal image of the pastern of an adult horse with lameness associated with the distal left front limb. No abnormalities were present on radiographs of the distal limb. The deep digital flexor tendon has abnormal contour. Effusion palmar to the tendon is increased (*arrows*). **B**, Proton density transverse image at the level of the distal pastern. An abnormally enlarged medial bundle of the deep digital flexor tendon is visible (*white arrows*). The lateral bundle of the deep digital flexor appears normal. The increased effusion surrounding the tendon is apparent (*black arrows*). DDF, Deep digital flexor tendon.

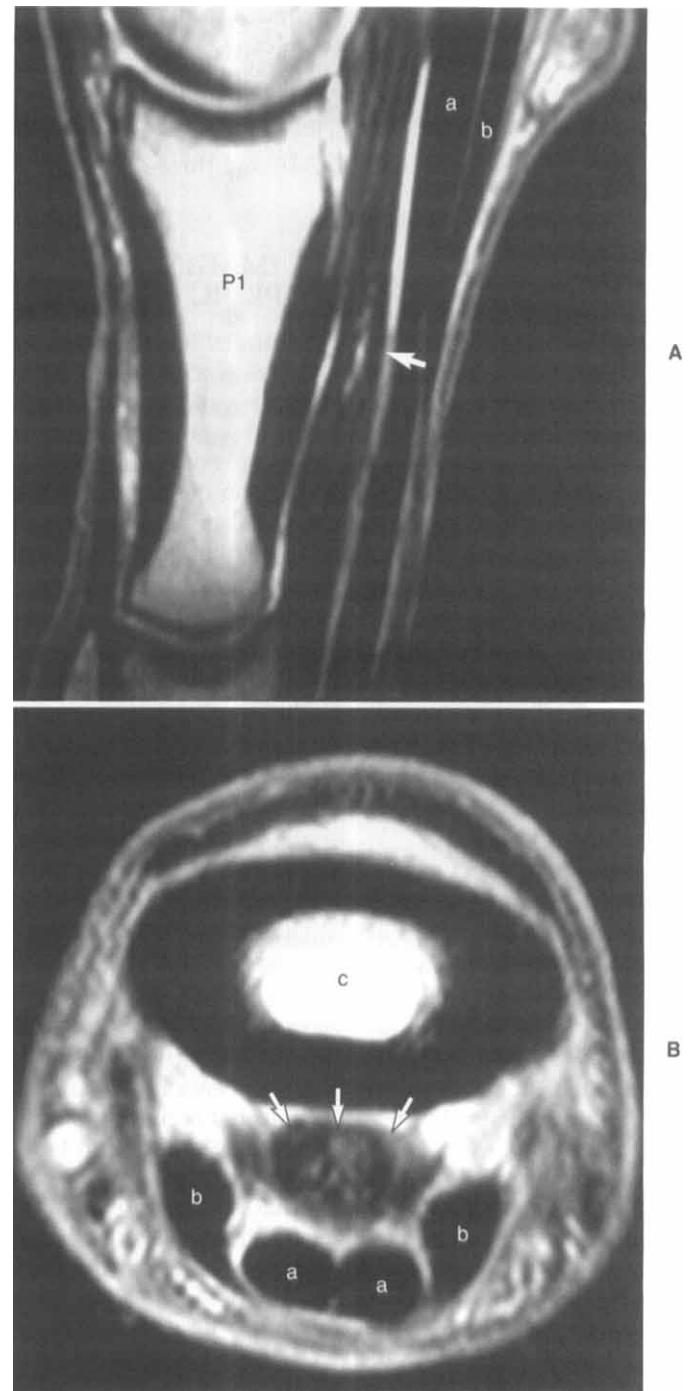


Figure 10.5-3 **A**, T2-weighted sagittal image of the midpalmar pastern of an adult Quarter Horse with chronic lameness localized to the distal limb. No abnormalities were noted on radiographs. Within the straight distal sesamoidean ligament is thickening and increased signal (*arrow*). *a*, Deep digital flexor tendon; *b*, superficial digital flexor tendon; *P1*, first phalanx. **B**, Proton density transverse image of the midpalmar pastern. The straight distal sesamoidean ligament is thickened and has increased internal signal (*arrows*). *a*, Medial and lateral bundles of the deep digital flexor tendon; *b*, medial and lateral branches of the superficial digital flexor tendon; *c*, medullary cavity of *P1*.

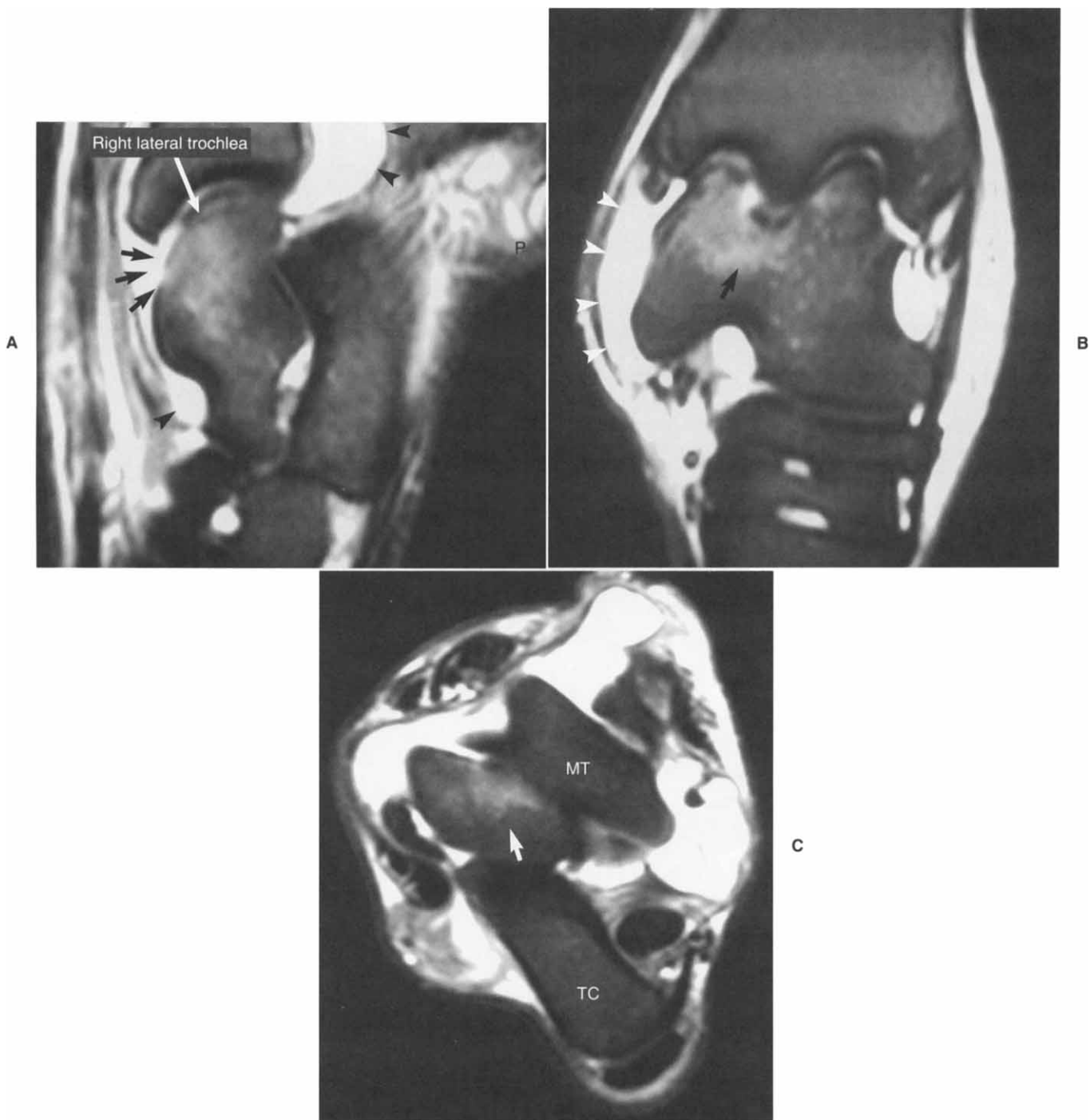


Figure 10.5-4 **A**, Fat-suppressed sagittal image of the lateral trochlear ridge of a horse with lameness and effusion localized to the right tarsal joint. Radiographs of the joint were unremarkable other than effusion of the tibial-tarsal joint. A large region of abnormal high signal represents bone contusion in the subchondral bone of the lateral trochlear ridge (*black arrows*). A large amount of synovial effusion is present (*black arrowheads*). **B**, Fat-suppressed dorsal image of the tibial tarsal joint. The subchondral region of high signal within the lateral trochlear ridge is readily apparent (*black arrow*). The joint effusion is noted within the lateral joint compartment on this image (*white arrowheads*). **C**, Fat-suppressed transverse image of the trochlear ridges. The abnormal region of high signal contusion in the subchondral bone of the lateral trochlear ridge is compared with the normal signal of the medial trochlear ridge (*arrow*). MT, Medial trochlear ridge of the talus; TC, tuber calcaneus.

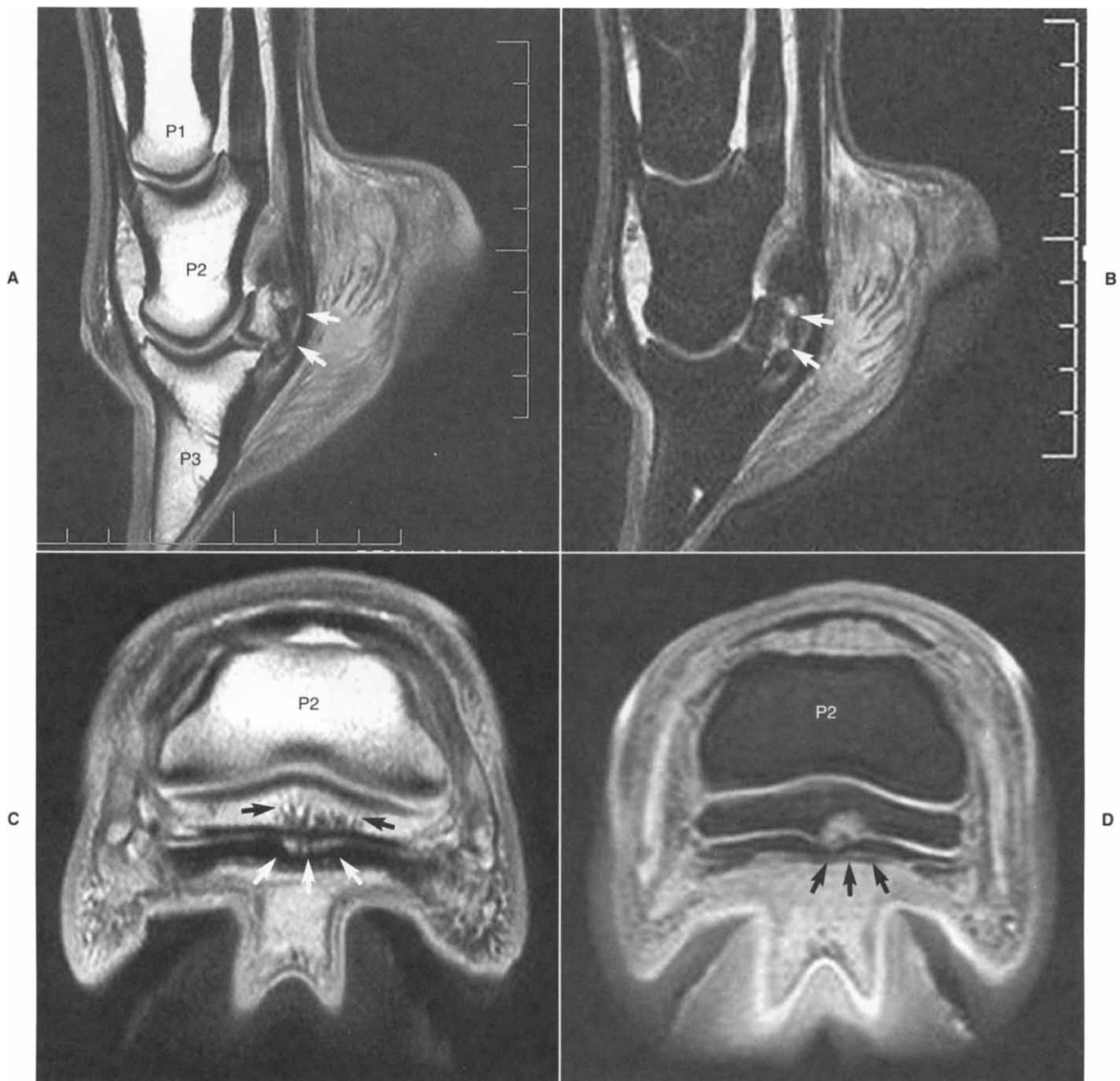


Figure 10.5-5 **A**, Proton density sagittal image of the distal foot and the navicular bone in a horse with lameness localized to the heel bulb region. Radiographs of the navicular bone were normal. Large cortical defects are present along the flexor surface of the navicular bone (arrows). P1, First phalanx; P2, second phalanx; P3, third phalanx. **B**, Fat-suppressed sagittal image of the same section as A. The navicular bone has increased synovial invaginations and medullary signal (arrows). **C**, Proton density transverse image of the navicular bone. Large hypointense cortical defects are found along the flexor surface of the navicular bone (black arrows). The deep digital flexor tendon has increased signal adjacent to the navicular bone (white arrows). P2, Second phalanx. **D**, Fat-suppressed transverse image of the same section as C. The navicular bone has a large inflammatory focus surrounding the erosions on the flexor cortex with adhesions to the deep digital flexor tendon (arrows). P2, Second phalanx.

diographic confirmation of intraarticular or bursal administrations. MRI arthrography is useful for delineation of focal cartilage erosions or osteochondral defects that communicate into the joint.

LIMITATIONS OF MAGNETIC RESONANCE IMAGING

Several important limitations exist to the use of MRI that must be considered in equine patients. MRI systems capable of imaging live horses are available at only a few veterinary institutions worldwide. The requirement of general anesthesia and the time required for scanning must be an acceptable risk for each patient. Routine orthopedic MRI examinations require between 30 and 90 minutes, depending on how many areas are examined and how many sequences are required for each area. Future development of specialized MRI systems capable of imaging a standing horse would avoid the requirement for general anesthesia and will expand applications and acceptance. The cost may be prohibitive for many horse owners.

The full spectrum of applications of MRI in equine orthopedic cases has yet to be determined. Optimal imaging sequences and scanning parameters still must be determined for equine orthopedic applications. With the multiple MRI techniques in orthopedic diseases in humans as an indicator for potential applications in horses, the future of MRI in horses is exciting.

Supplemental Readings

- Hoskinson JH, Tucker RL, Lillich J et al: Advanced diagnostic imaging modalities available at the referral center. *Vet Clin North Am Equine Pract* 1997; 13:601-612.
- Martinelli MJ, Baker GJ, Clarkson RB et al: Magnetic resonance imaging of degenerative joint disease in a horse: a comparison to other diagnostic techniques. *Equine Vet J* 1996; 28:410-415.
- Tucker RL, Sande RD: Computed tomography and resonance imaging in equine musculoskeletal conditions. *Vet Clin North Am Equine Pract* 2001; 17:145-157.
- Widmer WR, Buckwater KA, Fessler JF et al: Use of radiography, computed tomography and magnetic resonance imaging for evaluation of navicular syndrome in the horse. *Vet Radiol Ultrasound* 2000; 41:108-116.

CHAPTER 10.6

Biomarkers of Joint Disease

R. CLARK BILLINGHURST
Fort Collins, Colorado

The equine practitioner currently depends on clinical and radiographic signs to diagnose joint disease in the horse. Often little correlation exists between the two, unfortunately, and radiographic evidence of joint damage often does not appear until the disease process has progressed far enough that considerable and permanent damage has already occurred. If the practitioner could identify disease activity before irreversible changes have occurred within the tissues of the joint, it is conceivable that measures could be taken to avoid further destruction and restore joint functionality. Moreover, if this assessment could be made with a simple blood, urine, or synovial fluid test, then this evaluation could become a routine and widely used procedure to monitor the development and training of horses. This evaluation has the potential to diminish the tremendous losses caused annually by joint disease.

BIOMARKERS

The terms *biomarker*, *biochemical marker*, and *molecular marker* have all been used to describe either direct or indirect indicators of abnormal skeletal tissue turnover. These markers are generally molecules that are the normal products and byproducts of the metabolic processes occurring within the skeleton. In disease, alterations occur in the bal-

ance between the anabolic and catabolic processes within skeletal tissues; thus the concentrations of biomarkers may either increase or decrease. In joint disease, these molecules may appear in the synovial fluids of the affected joints when they are of articular cartilage, meniscal, ligamentous, or synovial origin. If the underlying subchondral bone is involved, the molecules of osseous origin will usually be cleared directly into the bloodstream. Many of these molecules will undergo further processing in the liver and/or kidneys and some may even be excreted in the urine in a concentrated form (Figure 10.6-1). All in all, the ability to identify and measure these substances in body fluids offers researchers and practitioner alike the opportunity to use these molecules as biomarkers of joint disease.

WHY BIOMARKERS ARE USED

Measurement of the levels of biomarkers of joint disease in the body fluids of horses can be used in one of the following ways:

1. As a diagnostic test to differentiate between affected and nonaffected joints/animals
2. As a prognostic test to identify joints/animals likely to show rapid progression or to predict response to therapy

diographic confirmation of intraarticular or bursal administrations. MRI arthrography is useful for delineation of focal cartilage erosions or osteochondral defects that communicate into the joint.

LIMITATIONS OF MAGNETIC RESONANCE IMAGING

Several important limitations exist to the use of MRI that must be considered in equine patients. MRI systems capable of imaging live horses are available at only a few veterinary institutions worldwide. The requirement of general anesthesia and the time required for scanning must be an acceptable risk for each patient. Routine orthopedic MRI examinations require between 30 and 90 minutes, depending on how many areas are examined and how many sequences are required for each area. Future development of specialized MRI systems capable of imaging a standing horse would avoid the requirement for general anesthesia and will expand applications and acceptance. The cost may be prohibitive for many horse owners.

The full spectrum of applications of MRI in equine orthopedic cases has yet to be determined. Optimal imaging sequences and scanning parameters still must be determined for equine orthopedic applications. With the multiple MRI techniques in orthopedic diseases in humans as an indicator for potential applications in horses, the future of MRI in horses is exciting.

Supplemental Readings

- Hoskinson JH, Tucker RL, Lillich J et al: Advanced diagnostic imaging modalities available at the referral center. *Vet Clin North Am Equine Pract* 1997; 13:601-612.
- Martinelli MJ, Baker GJ, Clarkson RB et al: Magnetic resonance imaging of degenerative joint disease in a horse: a comparison to other diagnostic techniques. *Equine Vet J* 1996; 28:410-415.
- Tucker RL, Sande RD: Computed tomography and resonance imaging in equine musculoskeletal conditions. *Vet Clin North Am Equine Pract* 2001; 17:145-157.
- Widmer WR, Buckwater KA, Fessler JF et al: Use of radiography, computed tomography and magnetic resonance imaging for evaluation of navicular syndrome in the horse. *Vet Radiol Ultrasound* 2000; 41:108-116.

CHAPTER 10.6

Biomarkers of Joint Disease

R. CLARK BILLINGHURST
Fort Collins, Colorado

The equine practitioner currently depends on clinical and radiographic signs to diagnose joint disease in the horse. Often little correlation exists between the two, unfortunately, and radiographic evidence of joint damage often does not appear until the disease process has progressed far enough that considerable and permanent damage has already occurred. If the practitioner could identify disease activity before irreversible changes have occurred within the tissues of the joint, it is conceivable that measures could be taken to avoid further destruction and restore joint functionality. Moreover, if this assessment could be made with a simple blood, urine, or synovial fluid test, then this evaluation could become a routine and widely used procedure to monitor the development and training of horses. This evaluation has the potential to diminish the tremendous losses caused annually by joint disease.

BIOMARKERS

The terms *biomarker*, *biochemical marker*, and *molecular marker* have all been used to describe either direct or indirect indicators of abnormal skeletal tissue turnover. These markers are generally molecules that are the normal products and byproducts of the metabolic processes occurring within the skeleton. In disease, alterations occur in the bal-

ance between the anabolic and catabolic processes within skeletal tissues; thus the concentrations of biomarkers may either increase or decrease. In joint disease, these molecules may appear in the synovial fluids of the affected joints when they are of articular cartilage, meniscal, ligamentous, or synovial origin. If the underlying subchondral bone is involved, the molecules of osseous origin will usually be cleared directly into the bloodstream. Many of these molecules will undergo further processing in the liver and/or kidneys and some may even be excreted in the urine in a concentrated form (Figure 10.6-1). All in all, the ability to identify and measure these substances in body fluids offers researchers and practitioner alike the opportunity to use these molecules as biomarkers of joint disease.

WHY BIOMARKERS ARE USED

Measurement of the levels of biomarkers of joint disease in the body fluids of horses can be used in one of the following ways:

1. As a diagnostic test to differentiate between affected and nonaffected joints/animals
2. As a prognostic test to identify joints/animals likely to show rapid progression or to predict response to therapy

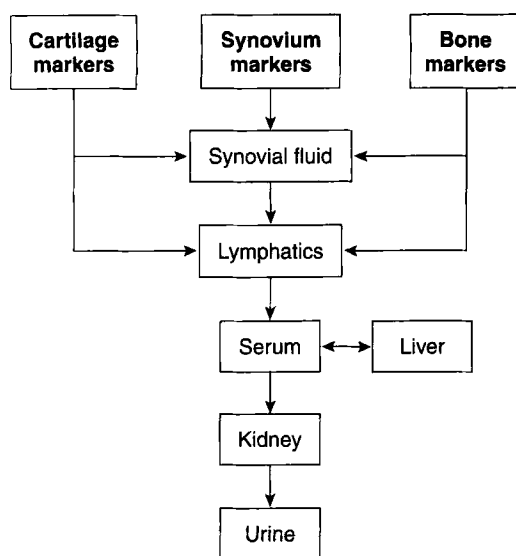


Figure 10.6-1 The clearance of biomarkers from joints for detection in body fluids.

3. As an evaluative test to assess disease severity, monitor change in disease status, or to monitor response to therapy

In each case, the validity of a marker as a measure of joint disease is the critical determinant of the efficacy of that test. Questions asked in the assessment of the validity of each biomarker include the following:

- Is it biologically credible?
- Is it sensitive to changes in disease status?
- Does it predict/correlate with the gold standard for the disease?
- Is it relevant across multiple stages of disease?

Unfortunately no such marker currently exists in any species. Nevertheless some promising candidates have been identified and are being evaluated for use in human and equine joint disease.

WHICH BODY FLUID TO SAMPLE FOR BIOMARKERS

The body fluid of choice for the practitioner would be blood (serum) because it is easy to obtain, is of a relatively constant volume in the body, and is a good indicator of systemic changes within the musculoskeletal system of the animal. In the case of disease in a single joint, however, unless it is a large joint it is less likely that increases in marker levels will be detectable in blood. Moreover, the blood level of many markers is dependent on their clearance rate from the joint, as well as liver and kidney function. Therefore synovial fluid may be the fluid of choice for the measurement of marker levels in the assessment of single joint disease. Because of the lack of blood vessels in articular cartilage, the products of the metabolic processes that occur within this tissue are released directly into the synovial fluid, resulting in higher concentrations and half-lives for these markers in synovial fluid than would exist in blood. However, the issue that practitioners must ad-

dress when analyzing synovial fluid levels of markers is that these levels are dependent on volume changes within the joint, and inflammation will affect the clearance from the joints of most markers. Synovial fluid is also more difficult to obtain than blood, especially if required on a continuous basis.

Measurement of the urine concentrations of markers such as specific collagen degradation products (crosslinks) is often performed in humans but offers no advantages over blood or synovial fluid for the measurement of most other markers of skeletal tissue metabolism in the horse. Urine is also usually more difficult to obtain in the horse than is blood or synovial fluid.

WHICH BIOMARKERS TO MEASURE

When deciding which markers should be evaluated for a specific condition, practitioners must determine those tissues and metabolic products that may be a part of the pathogenesis of the disease. In joint disease, practitioners are concerned with the integrity and functionality of the articular cartilage that lines the surfaces of the bones forming each joint, the supporting subchondral bone, the synovial membrane and the synovial fluid it produces, and any intraarticular ligamentous or meniscal tissues that may be present. In the text that follows, putative markers of joint disease from cartilage, bone, and synovium will be described separately. These markers are summarized in Table 10.6-1, where they are classified by the tissue/molecule of their origin and as either an indicator of the synthesis (anabolism) or breakdown (catabolism) of that tissue/molecule. These markers have also been listed in Table 10.6-2, along with the type, name, and manufacturer (if applicable) of the assay(s) used to measure their levels in horses.

CARTILAGE DEGRADATION MARKERS

The two main proteins that compose the matrix of articular cartilage are type II collagen and aggrecan molecules (proteoglycans). When damage to articular cartilage occurs, there is an increase in the tissue release of degradation products of both type II collagen and aggrecan. It appears that aggrecan loss precedes collagen damage and that, after a certain threshold of loss is reached, there is irreversible damage to the cartilage with the loss of type II collagen. Therefore the ability to identify early changes in the turnover of these aggrecan molecules would allow the practitioner the opportunity to detect articular cartilage damage before it becomes irreparable.

Aggrecan Assays

Sulfated Glycosaminoglycans

Historically the release of sulfated glycosaminoglycan (sGAG) fragments into synovial fluid has been measured with a biochemical assay that uses the dye dimethylmethylene blue (DMMB). This assay identifies all sGAGs present in synovial fluid regardless of their origin (i.e., menisci, articular cartilage, and synovial membrane). Synovial fluid sGAG levels have been inconsistent in differentiating osteoarthritic (OA) from normal equine joints.

Table 10.6-1
Body Fluid Biomarkers for the Assessment of Joint Tissue Turnover in Horses

Tissue/Molecules	Synthesis	Breakdown
Cartilage		
Aggrecan	Chondroitin sulfate epitopes (CS-846)	Sulfated glycosaminoglycans (sGAGs)
Type II collagen	Procollagen propeptides (C-propeptide)	Keratan sulfate epitopes (5D4, AN9PI)
Other	Matrix metalloproteinases (MMPs)	Core protein epitopes and neoepitopes
	Tissue inhibitor of matrix metalloproteinases (TIMP)	Cleavage-site neoepitopes (234CEQ)
		Denatured collagen (COL2-3/4m)
		Pyridinium crosslinks (PYD)
		Telopeptides (Col2CTx)
		Cartilage oligomeric matrix protein (COMP)
		MMPs
Bone		
Type I collagen	Procollagen propeptides (PICP)	Cleavage-site neoepitopes (COL2-3/4C _{short})
Noncollagen proteins	Bone-specific alkaline phosphatase (BALP)	Pyridinium crosslinks (DPYD, PYD)
	Osteocalcin	Telopeptides (CTx, ICTP)
Synovium		
Type III collagen	Procollagen propeptide (PIIINP)	Cytokines (IL-1 β , TNF- α , IL-6)
Noncollagen proteins	Hyaluronic acid (HA)	Eicosanoids (PGE ₂)
	COMP	MMPs
	MMPs	
	TIMP	

IL, Interleukin; TNF, tumor necrosis factor; PGE₂, prostaglandin E₂.

Early studies showed significantly increased levels of sGAG in the urine, serum, and/or synovial fluid of horses with OA; however, a later report noted no significant differences in the synovial fluid levels of sGAG between OA and normal joints. Moreover, it has been shown that sGAG levels are significantly different in synovial fluids from different normal joints of the horse, and this must be considered if one is to use sGAG levels to evaluate and compare joint disease in different joints.

Chondroitin Sulfate

Byproducts of aggrecan degradation that have been measured include proteoglycan fragments that contain "epitopes" that allow for their immunologic detection with antibodies. The predominant sGAG in aggrecan is chondroitin sulfate (CS). Antibodies have been developed to recognize both native epitopes on CS and neoepitopes (new epitopes) created by the digestion of CS with enzymes. Very little work has been done with these antibodies in assaying body fluids of horses.

Keratan Sulfate

Keratan sulfate (KS) is the other major sGAG bound to the protein core of the proteoglycans that form the aggrecan molecule. As described above for total sGAG levels, conflicting reports have been published concerning the relationship between the levels of KS in equine body fluids and joint disease, and it has also been shown that KS levels, like sGAG, are significantly different in synovial fluids from different normal joints of the horse. In an early re-

port, synovial fluid and serum levels of KS were significantly increased in equine joints with OA compared with normal joints. However, a subsequent study indicated that there were significantly lower levels of KS in synovial fluids from joints with clinically active OA versus normal joints. A study that involved horses with varying degrees of unilateral osteochondral fragmentation of the carpus reported no significant differences in the serum and synovial fluid levels of KS between normal horses and horses with affected joints. However, significantly lower levels of KS were detected in synovial fluids from joints with osteochondrosis compared with fluids from normal joints. Similar discrepancies have been reported in human studies evaluating the use of KS as a marker of joint disease, and it appears at present that it has limited, if any, use for the routine monitoring of body fluids for joint disease in any species.

Aggrecan Core Protein

Antibodies have been developed against native epitopes in the protein core of aggrecan and against neoepitopes created by the digestion of the aggrecan core with matrix metalloproteinases (MMPs) and aggrecanases, which are enzymes involved in the metabolic turnover of aggrecan in health and disease. One study that used an antibody recognizing native epitopes on equine aggrecan showed a statistically lower concentration of aggrecan in the synovial fluid from the middle carpal joints of horses with moderate OA compared with the levels in fluids from normal middle carpal joints. No reports have been published

Table 10.6-2
Currently Available Biomarker Assays of Joint Tissue Metabolism in Horses

Tissue	Biomarker	Type of Assay	Name of Assay	Company
Cartilage	C-propeptide of type II procollagen	EIA	CPIL	HDM Diagnostics
	Chondroitin sulfate (CS) epitope 846	EIA	CS-846	HDM Diagnostics
	Cleaved type II collagen (234CEQ)	EIA	234CEQ	None
	Sulfated glycosaminoglycan (sGAG)	Colorimetric	DMMB	None
	Keratan sulfate (KS)	EIA	5D4	None
Bone	Cartilage oligomeric matrix protein (COMP)	EIA	None	None
	C-propeptide of type I procollagen	RIA	PICP	Orion Diagnostica
	Bone-specific alkaline phosphatase	EIA	Alkphase-B	Quidel Corporation
	Osteocalcin	EIA	NovoCalcin	Quidel Corporation
		RIA	Osteocalcin	Diasorin, Inc.
	Cleaved type I & II collagen (COL2-3/4C _{short})	EIA	COL2-2/3C _{short}	HDM Diagnostics
	C-telopeptide of type I collagen (CTX)	RIA	ICTP	Orion Diagnostica
		EIA	Serum CrossLaps	Osteometer BioTech
	Deoxypyridinoline crosslinks (DPYD)	EIA	Pyrilinks-D (urine)	Quidel Corporation
		EIA	Total Dpd (serum/urine)	Quidel Corporation
Synovium	Pyridinium crosslinks (PYD and DPYD)	EIA	Pyrilinks (urine)	Quidel Corporation
	Pyridinoline (PYD)	EIA	Serum Pyd (serum)	Quidel Corporation
	N-propeptide of type III procollagen	RIA	PIIINP	Orion Diagnostica
	Hyaluronic acid (HA)	Colorimetric	Alcian Blue Analysis	None
	COMP	EIA	None	None
	Eicosanoids (PGE ₂)	EIA	Correlate-EIA	Assay Designs, Inc.
	Cytokines (IL-1 β , TNF- α , IL-6)	EIA	Correlate-EIA	Assay Designs, Inc.
	Matrix metalloproteinases (MMP)	EIA	Biotrak*	Amersham
	and tissue inhibitor of matrix metalloproteinases (TIMP)	Activity assays	None	None

EIA, Enzyme immunoassay; RIA, radioimmunoassay.

NOTE: Cross-reactivity of the human assay kits has not been proven in the horse.

on the use of the aggrecan neopeptide antibodies in assaying body fluid samples from horses.

Collagen Assays

Cleaved Type II Collagen

Type II collagen comprises 90% to 95% of articular cartilage "collagen" and it is believed that the increased turnover and destruction of the structural collagen framework within the cartilage matrix signals the irreversible stages of joint disease. The initial degradation of fibrillar collagens usually occurs as a result of the action of collagenases. This digestion results in two collagen fragments of 3/4 and 1/4 lengths with newly created ends at the cleavage site. These neopeptides are recognized by antibodies produced to react with the specific amino acid sequences at the newly created ends and their levels can serve as indicators of collagenase activity and collagen breakdown. The COL2-3/4C_{short} antibody recognizes collagenase-cleaved fragments of both type I and II collagens, so it is not specific to cartilage collagen. However,

an antibody named 234CEQ has been developed that is specific for the collagenase-cleaved 3/4 fragments of type II collagen of the horse, and preliminary studies suggest that it may prove useful in assaying equine body fluids for abnormalities in type II collagen turnover, as may occur in osteochondrosis. An assay (type II collagen neopeptide [TIINE]) that incorporates two antibodies (one very similar to the COL2-3/4C_{short} antibody) has been used to detect collagenase-cleaved fragments of type II collagen in the urine of humans, with significant differences reported between patients with OA and control subjects.

Denatured Collagen

After the triple helical collagen molecules are cleaved by collagenases, the individual chains begin to unwind or denature, exposing previously hidden amino acid sequences. Antibodies exist that detect such hidden epitopes that are specific for denatured type II collagen (COL2-3/4m). One study in horses reported no differences in the levels of denatured type II collagen in synovial fluids from joints with OA versus normal joints of horses.

Collagen Crosslinks

Mature collagen molecules possess crosslinks that provide cohesiveness and stability to the collagenous meshwork. With collagen degradation, these crosslinks are released from the tissue. Although the pyridinoline (PYD) crosslinks predominate in cartilage, because they are the major crosslinks in all connective tissues they do not provide specificity as a cartilage degradation marker. Another pyridinium crosslink called deoxypyridinoline (DPYD) is found in large amounts in mineralized tissue and will be described further as a marker of bone collagen degradation. Assays (Col2 CTx) have been developed that take advantage of the fact that these crosslinks are often contained in degraded collagen fragments that appear in urine, and antibodies recognizing specific epitopes in these crosslinked collagen chains can incur collagen type specificity. These assays show promise in human studies but no published reports currently exist on their use in horses.

Other Assays

Cartilage Oligomeric Matrix Protein

Cartilage oligomeric matrix protein (COMP) was named for its original discovery and abundance in cartilage, but it has since been found in other tissues including tendon, synovium, and meniscus. The precise role of COMP in cartilage is not known but increased levels have been noted in the synovial fluids and sera of humans with early OA; these levels have tended to increase with disease progression. COMP levels in the synovial fluids and sera of horses with both aseptic and septic joint disease have been shown to be significantly lower than the levels in fluids from normal horses.

Matrix Metalloproteinases

The matrix metalloproteinases (MMPs) are enzymes produced by chondrocytes that can degrade most of the components of the cartilage matrix. Their natural inhibitors, tissue inhibitor of metalloproteinases (TIMPs), regulate the activity of the MMPs. Cells within the synovial membrane and invading inflammatory cells produce both MMPs and TIMPs, so they are not specific to cartilage. Equine studies have focused on one subgroup of the MMP family called the *gelatinases* (i.e., MMP-2 and MMP-9). As gelatinases, their main proteolytic activity is the digestion of denatured collagen (gelatin), but they degrade aggrecan molecules as well. Elevated levels of both gelatinases, in particular MMP-9, have been detected in synovial fluids from both septic and aseptic joint disease compared with the levels in fluids from normal equine joints. A significantly higher activity of MMP-3 or stromelysin-1 has also been found in fluids from joints with OA compared with normal joint fluids.

MMP-3 can degrade many of the components of cartilage matrix, in addition to being an activator of many of the other MMPs. A similar increase was noted for TIMP levels in synovial fluid from aseptic but not septic equine joints. Unfortunately, the assays used to quantitate these MMPs are not easy to perform in a clinical setting and all currently available commercial immunoassays for MMPs

have not been validated as cross-reacting with the MMPs of the horse. For these reasons the routine assaying of body fluids for MMP and TIMP levels in horses is not currently practical for the practitioner.

CARTILAGE SYNTHESIS MARKERS

Collagen Assays

Type II Procollagen Propeptide

Type II collagen is secreted by chondrocytes as individual "procollagen" chains that are further processed after triple helix formation by the enzymatic cleavage of the "propeptides" at both ends of the procollagen chains. It has been shown that the rate of the release of the propeptide at the carboxy-terminus, the C-propeptide, is proportional to the rate of type II collagen synthesis. Moreover, studies in humans have reported increased levels of C-propeptide in synovial fluids of OA patients but decreased levels in their serum. Increased levels of the C-propeptide of type II collagen have also been detected by using similar immunoassays (C-propeptide [CPII]) in the synovial fluids and sera of horses with osteochondrosis (OC), with a direct relationship between the serum levels of CPII and the severity of disease. The potentially harmful effects of repeated intraarticular corticosteroid administration on cartilage metabolism and joint health in the horse were suggested by a significant decrease in the levels of CPII in synovial fluids from the steroid injected joints. This decrease persisted for 1 month after the last injection compared with levels in control joints.

Aggrecan Assays

Chondroitin Sulfate

Large, newly synthesized aggrecan molecules appear to have an epitope called 846 that can be measured to monitor aggrecan synthesis. This epitope progressively disappears from cartilage with aging but reappears in joints with OA and increases in synovial fluid following joint injury, perhaps reflecting a repair response. In horses with osteochondral fragmentation, significantly higher synovial fluid and serum levels of the 846 epitope were found compared with control horses. Coupled with elevated CPII levels in these horses, the serum concentration of both these epitopes was shown to correctly predict the occurrence of osteochondral fragmentation 79% of the time. In equine osteochondrosis, significantly lower synovial 846 epitope levels were detected, a finding that suggests impairment of aggrecan synthesis in this disease.

BONE DEGRADATION MARKERS

Bone markers may not provide much useful information in terms of joint disease, especially in the early stages where markers may prove to be the most useful in identifying joints and/or horses at risk of disease. In fact, a major use of bone markers in human medicine involves systemic metabolic bone disorders such as osteoporosis and Paget's disease, conditions not described in the horse. Nevertheless, in developmental disorders

such as osteochondrosis or joint disease, bone markers may predict progression and prove useful in monitoring response to treatment. Bone markers may also be important in assessing bone remodeling in training, identifying abnormalities in the bones of exercising horses before they progress into potentially serious injuries, such as fractures.

Collagen Assays

Cleaved Type I Collagen

The COL2-3/4C_{short} antibody recognizes collagenase-cleaved fragments of both type I and II collagens, so it is not specific to bone collagen, but when this antibody is used in combination with the previously described 234CEQ antibody that is specific for equine type II collagen, a clear picture emerges of the relative breakdown of type I collagen. Its use in equine studies has been restricted to measurement of serum levels in foals predisposed to OC. Studies demonstrated significantly increased levels of type I collagen and less type II collagen turnover during the first 5 months of life in those foals with more numerous and severe lesions.

Collagen Crosslinks

The major collagen of bone is type I, and similar to type II collagen of cartilage, the type I molecules are stabilized by the pyridinium crosslinks, PYD and DPYD, which are both released from bone during its degradation. The DPYD crosslinks are almost exclusively found in bone and may therefore be the best crosslink to monitor bone turnover. Immunoassays exist that can be used to measure DPYD in equine urine or serum (Pyrilinks-D and total Dpd, Quidel Corp., San Diego, Calif.). Reports on the use of these immunoassays in horses are limited and mainly describe a decrease in urinary DPYD levels with age and exercise.

Another product of type I collagen degradation are the crosslinked ends or "telopeptides" that can be measured in serum by using commercially available immunoassays. An assay for the carboxy-terminal-linked telopeptide of type I collagen (ICTP) has been used in equine studies to show that serum ICTP levels, like most other bone markers, decrease with age and differ between breeds. Elevated ICTP levels have been reported in horses with developmental orthopedic disease (DOD) compared with age-matched controls. Further studies are necessary to determine if this bone marker has any potential use in equine joint disease.

Another crosslink assay that can be used in horses is the C-telopeptide crosslink (CTX) assay. Unlike most other bone markers, serum CTX levels appear to increase in foals with increasing age (unpublished data). More studies that assay CTX levels need to be performed in the horse to determine its value as a biomarker of joint disease.

Noncollagenous Protein Assays

Potential noncollagenous protein markers of bone degradation exist including bone sialoprotein (BSP) and tartrate-resistant acid phosphatase (TRAP), but no assays are currently available for their detection in the horse.

BONE SYNTHESIS MARKERS

Collagen Assays

Type I Procollagen Propeptide

As with type II collagen, type I procollagen of bone also possesses propeptides that are cleaved and released from the collagen molecules upon fibril formation. Assays exist for both the N-terminal (PINP) and C-terminal (PICP) propeptides, but only the latter is currently applicable to horses. Serum PICP levels decrease with age and increase with exercise in horses. Reduced serum levels of PICP were detected in horses with DOD compared with age-matched controls. However, practitioners must exercise caution in interpreting the results of PICP assays, because type I collagen is also found in skin, muscle, blood vessels, and synovium, all of which may contribute to systemic PICP levels.

Noncollagenous Protein Assays

Bone-Specific Alkaline Phosphatase

This isoform of alkaline phosphatase is produced by bone cells (osteoblasts) during bone formation, and serum levels of this substance have been measured in horses with the use of various assays. As with PICP, an inverse relationship exists between age and the serum levels of bone-specific alkaline phosphatase (BALP) in the horse, and serum levels increase with exercise. Significantly higher synovial fluid levels of BALP have been reported in clinically affected OA joints than in the contralateral joints of horses, with a strong positive correlation between BALP levels and the degree of articular cartilage damage.

Osteocalcin

Osteocalcin is also produced by the osteoblasts and is an accepted marker of bone formation. In the circulatory system it is present as the intact molecule and as fragments, and the assays for osteocalcin differ as to which of these they detect. It is very important that serum samples are processed and stored at -20°C soon after collection because the molecule is very labile and will rapidly degrade, thereby leading practitioners using assays that only detect intact osteocalcin to underestimate blood levels. Many reports that describe osteocalcin levels in normal horses have noted an inverse correlation with age, gender differences, daily and seasonal fluctuations, and differences with exercise. Studies of serum osteocalcin levels in regard to equine joint disease are rare, but preliminary studies in osteochondrosis and osteochondral fragmentation suggest limited value in these conditions.

SYNOVIUM MARKERS

The synovial membrane that lines the joints is responsible for supplying the synovial fluid that nourishes, lubricates, and protects articular soft tissues. This fluid also contains the metabolic products of the intraarticular tissues that it bathes, including the cartilage, ligaments, menisci, and the synovial membrane itself. In inflammation and disease there can also be an increase in the cellular component of the synovial membrane and fluid, and the products of these invading cells can magnify the degradative response.

Synovium Degradation Markers

Direct Markers

No specific and direct markers of synovial membrane degradation have been established for use in the horse. However, the urinary Glc-Gal-PYD crosslink marker looks promising as a marker of synovial degradation in humans.

Indirect Markers

Indirect markers include the mediators and products of the inflammatory processes that occur within the synovium in disease, such as the MMPs, cytokines, and eicosanoids. Although the synovial membrane is a significant source of all of these inflammatory mediators, they are not specific to this tissue. Moreover, assays either do not exist for the horse or, if they do, are extremely complicated to perform. Conflicting reports on the levels of some inflammatory mediators may be a reflection of the different assays used between the studies. For example, one group of researchers using a bioassay showed no correlation between the synovial fluid levels of the cytokine, tumor necrosis factor- α (TNF- α), and degree of joint damage, but another group using an immunoassay for human TNF- α described the synovial fluid levels of TNF- α as a good predictor of joint disease. In this latter study, the cytokines interleukin-1 (IL-1) and interleukin-6 (IL-6) were also shown to be predictors of joint disease, but again this was determined with immunoassays developed for humans that have not been proved to react to the equine cytokines.

The eicosanoid prostaglandin E_2 (PGE $_2$) can be released from synovial cells and chondrocytes and has been described as a high predictor of joint disease in the horse, but the validity of the immunoassay for equine fluids needs to be confirmed before it can be recommended as a screening test for any joint disease.

Synovium Synthesis Markers

Type III Procollagen Propeptide

The synovial membrane, unlike the articular cartilage and bone, contains type III collagen and therefore any products of its turnover within the synovial fluid may be assumed to be of a synovial membrane origin. As with type I and II procollagens, the N-propeptide of type III collagen is cleaved during fibril formation and can be used as an indicator of collagen synthesis. An assay for the aminoterminal propeptide of type III procollagen (PIIINP) has shown very promising results in assessing synovial inflammation in human joint disease, and a recent report of its use in the horse describes a correlation between serum levels and weight gain.

Other Assays

Hyaluronan (Hyaluronic Acid)

Hyaluronic acid (HA) is a high-molecular weight GAG that is produced by synovial lining cells (fibroblasts) and is also found in aggrecan. Synovial fluid levels of HA have been assessed in numerous equine studies with conflicting results. In the majority of reports, lower levels of HA were found in fluids from arthritic joints compared with those from normal joints, whereas a couple of studies described no difference in HA levels between arthritic

and normal joints. Serum HA levels have been assessed in numerous human studies and generally increases are noted in patients with joint disease, but no reports exist of serum HA levels in equine arthritis. The routine measurement of HA levels is complicated by the fact that no commercially available HA assays currently exist.

Cartilage Oligomeric Matrix Protein

As described under the section on cartilage markers, cartilage oligomeric matrix protein (COMP) also produced by synovial cells, so that synovial fluid levels may reflect a substantial contribution from these cells.

CONCLUSION

This chapter reviews the molecules and the assays available to measure the levels of those molecules that are potential biochemical and immunologic markers of joint disease in the horse. It should be evident on reading this material that there are many candidates, and much work still needs to be done to identify the best indicators of the status of the equine joint. It is highly unlikely that one body fluid sample from one horse will be sufficient to define the health of that horse's joint(s). More realistically, a panel of markers may be needed to assess osteoarthritis, another to define the risk and severity of osteochondrosis, a third to predict the risk of fractures, and still another to assess the effects of training on the musculoskeletal system of the young racehorse.

For the practitioner, the question is how markers of bone, cartilage, and synovial tissue turnover can improve the identification and management of joint disease. In conjunction with more sensitive imaging devices, the use of markers of joint tissue degradation and synthesis will help to identify early reversible damage in joints, will predict progression, and will monitor the response to therapeutic intervention. Researchers are actively trying to identify more specific markers of articular cartilage damage in an attempt to better define joint disease, and improved and more sensitive assays are being developed to allow for the increased assessment of the levels of biomarkers in horses. These assays are becoming more user-friendly, but because of the need to standardize the tests to establish normal fluid levels in the horse, it will be more feasible for practitioners to send their fluid samples to centralized laboratories to be processed. As part of the standardization process sampling procedures will need to be well-defined, because as previously described, the levels of many of these markers are significantly influenced by such factors as age, breed, exercise, season, and liver and kidney function. The metabolism and clearance of the markers must be defined along with the contribution to body fluids of these molecules from nonarticular sources.

With that said, the use of biomarkers for the detection and monitoring of joint disease in the horse is an extremely exciting and realistically attainable goal. One must gain tremendous encouragement from the great advances made in human biomarker use—for example, the now routine procedure of measuring bone resorption markers to diagnose and to monitor the treatment re-

sponse in certain metabolic bone diseases. The ability to noninvasively assess the status of the musculoskeletal system at the molecular level is remarkable in its potential and worthy of the pursuit, given the potential long-term benefits to the horse.

Supplemental Readings

Garnero P, Rousseau JC, Delmas PD: Molecular basis and clinical use of biochemical markers of bone, cartilage, and synovium in joint diseases. *Arthritis Rheum* 2000; 43:953-968.

Lepage OM, Carstanjen B, Uebelhart D: Non-invasive assessment of equine bone: an update. *Vet J* 2001; 161:10-22.

Lohmander LS: What is the current status of biochemical markers in the diagnosis, prognosis and monitoring of osteoarthritis? *Baillieres Clin Rheumatol* 1997; 11:711-726.

Otterness IG, Saltarelli MJ: Using molecular markers to monitor osteoarthritis. In Tsokos GC, Moreland LW, Kammer GM et al (eds): *Modern Therapeutics in Rheumatic Diseases*, Totowa, NJ, Humana Press, 2001.

Ray CS, Poole AR, McIlwraith CW: Use of synovial fluid and serum markers in articular disease. In McIlwraith CW, Trotter GW (eds): *Joint Disease in the Horse*, Philadelphia, WB Saunders, 1996.

CHAPTER 10.7

Chronic Laminitis

ANDREW H. PARKS
Athens, Georgia

Chronic laminitis is defined by the presence of the mechanical collapse of the lamellae and displacement of the distal phalanx within the hoof capsule. This condition may occur as a direct sequel to acute laminitis (i.e., within the first 72 hours of onset of clinical signs) or as a sequel to subacute laminitis—the phase after the acute disease but without mechanical collapse. The fundamental difference between the pathogenesis of subacute laminitis and chronic laminitis is in the repair processes caused by displacement of the distal phalanx. This difference inevitably has consequences for treatment and prognosis.

PATHOPHYSIOLOGY OF CHRONIC LAMINITIS

Separation of the lamellae is a consequence of the severity of the original pathologic processes, inflammation, ischemia, thrombosis, and the mechanical stresses superimposed on the lamellae. Lamellar separation at any point around the circumference of the distal phalanx is therefore a balance between the severity of the underlying disease processes and the magnitude of lamellar stresses. The way in which the distal phalanx displaces is related to the distribution of lamellar separation around the circumference of the distal phalanx, and is therefore related to the distribution of the disease and stresses.

Weight-bearing stress is the greatest stress imposed on the lamellae. Added to weight-bearing stress is the stress caused by the moment around the distal interphalangeal joint. Also, as a horse moves, stress is concentrated in the dorsal hoof wall at breakover. Relatively uniform lamellar loss predisposes to distal displacement (sinking) of the entire distal phalanx within the hoof capsule. In contrast,

relatively greater lamellar disruption at the toe or either quarter will cause the distal phalanx to displace asymmetrically within the hoof capsule. When this loss is greatest dorsally, the result is dorsal capsular rotation. When one quarter or the other suffers greater injury, the distal phalanx displaces unilaterally (medial or lateral capsular rotation); this is a far less frequent scenario than dorsal capsular rotation. In reality it is unlikely that lamellar injury is confined to any one area around the perimeter of the foot; most horses display a combination effect.

Immediately after mechanical failure of the dorsal lamellae and rotation of the distal phalanx have occurred, the dorsal hoof wall is still straight and of normal thickness, and the space created by the separation is filled with hemorrhage and inflamed and necrotic tissue. The result of the repair process is that the space is variably filled with hyperplastic and hyperkeratinized epidermis and, to a lesser extent, hyperplastic dermis. Concurrent with lamellar repair is continued hoof growth and the development of the characteristic distortion of the dorsal wall. The severity of the distortion of the hoof wall varies with change in thickness and divergence from the parietal surface of the distal phalanx. The change in thickness of the hoof wall appears to be related to a change in the conformation of the coronary groove so that it is wider and shallower. At the onset of chronic laminitis, the eventual hoof capsule distortion is unpredictable. In most horses new wall growth from the coronary band is approximately parallel to the parietal surface of the distal phalanx, at least until it has reached the junction of the proximal and middle thirds of the hoof wall. At this juncture the proximal and distal portions of the hoof wall form two distinct angles with the ground. When the new hoof wall grows through the middle third of the dorsal hoof wall, a vary-

sponse in certain metabolic bone diseases. The ability to noninvasively assess the status of the musculoskeletal system at the molecular level is remarkable in its potential and worthy of the pursuit, given the potential long-term benefits to the horse.

Supplemental Readings

Garnero P, Rousseau JC, Delmas PD: Molecular basis and clinical use of biochemical markers of bone, cartilage, and synovium in joint diseases. *Arthritis Rheum* 2000; 43:953-968.

Lepage OM, Carstanjen B, Uebelhart D: Non-invasive assessment of equine bone: an update. *Vet J* 2001; 161:10-22.

Lohmander LS: What is the current status of biochemical markers in the diagnosis, prognosis and monitoring of osteoarthritis? *Baillieres Clin Rheumatol* 1997; 11:711-726.

Otterness IG, Saltarelli MJ: Using molecular markers to monitor osteoarthritis. In Tsokos GC, Moreland LW, Kammer GM et al (eds): *Modern Therapeutics in Rheumatic Diseases*, Totowa, NJ, Humana Press, 2001.

Ray CS, Poole AR, McIlwraith CW: Use of synovial fluid and serum markers in articular disease. In McIlwraith CW, Trotter GW (eds): *Joint Disease in the Horse*, Philadelphia, WB Saunders, 1996.

CHAPTER 10.7

Chronic Laminitis

ANDREW H. PARKS
Athens, Georgia

Chronic laminitis is defined by the presence of the mechanical collapse of the lamellae and displacement of the distal phalanx within the hoof capsule. This condition may occur as a direct sequel to acute laminitis (i.e., within the first 72 hours of onset of clinical signs) or as a sequel to subacute laminitis—the phase after the acute disease but without mechanical collapse. The fundamental difference between the pathogenesis of subacute laminitis and chronic laminitis is in the repair processes caused by displacement of the distal phalanx. This difference inevitably has consequences for treatment and prognosis.

PATHOPHYSIOLOGY OF CHRONIC LAMINITIS

Separation of the lamellae is a consequence of the severity of the original pathologic processes, inflammation, ischemia, thrombosis, and the mechanical stresses superimposed on the lamellae. Lamellar separation at any point around the circumference of the distal phalanx is therefore a balance between the severity of the underlying disease processes and the magnitude of lamellar stresses. The way in which the distal phalanx displaces is related to the distribution of lamellar separation around the circumference of the distal phalanx, and is therefore related to the distribution of the disease and stresses.

Weight-bearing stress is the greatest stress imposed on the lamellae. Added to weight-bearing stress is the stress caused by the moment around the distal interphalangeal joint. Also, as a horse moves, stress is concentrated in the dorsal hoof wall at breakover. Relatively uniform lamellar loss predisposes to distal displacement (sinking) of the entire distal phalanx within the hoof capsule. In contrast,

relatively greater lamellar disruption at the toe or either quarter will cause the distal phalanx to displace asymmetrically within the hoof capsule. When this loss is greatest dorsally, the result is dorsal capsular rotation. When one quarter or the other suffers greater injury, the distal phalanx displaces unilaterally (medial or lateral capsular rotation); this is a far less frequent scenario than dorsal capsular rotation. In reality it is unlikely that lamellar injury is confined to any one area around the perimeter of the foot; most horses display a combination effect.

Immediately after mechanical failure of the dorsal lamellae and rotation of the distal phalanx have occurred, the dorsal hoof wall is still straight and of normal thickness, and the space created by the separation is filled with hemorrhage and inflamed and necrotic tissue. The result of the repair process is that the space is variably filled with hyperplastic and hyperkeratinized epidermis and, to a lesser extent, hyperplastic dermis. Concurrent with lamellar repair is continued hoof growth and the development of the characteristic distortion of the dorsal wall. The severity of the distortion of the hoof wall varies with change in thickness and divergence from the parietal surface of the distal phalanx. The change in thickness of the hoof wall appears to be related to a change in the conformation of the coronary groove so that it is wider and shallower. At the onset of chronic laminitis, the eventual hoof capsule distortion is unpredictable. In most horses new wall growth from the coronary band is approximately parallel to the parietal surface of the distal phalanx, at least until it has reached the junction of the proximal and middle thirds of the hoof wall. At this juncture the proximal and distal portions of the hoof wall form two distinct angles with the ground. When the new hoof wall grows through the middle third of the dorsal hoof wall, a vary-

ing amount of deviation away from the parietal surface of the distal phalanx occurs. In other horses the newly formed hoof wall diverges from the parietal surface of the distal phalanx at the coronary band.

Displacement of the distal phalanx within the hoof capsule also causes the normal arch of the sole to drop. When the new dorsal hoof wall grows out and reaches the ground surface, the white line becomes wider, reflecting the increased space between the stratum medium of the hoof wall and the parietal dermis.

Complications during rehabilitation from chronic laminitis are common and include infection, perforation of the sole, contraction of the hoof, and contracture of the flexor apparatus. The combination of a cavity filled with necrotic tissue and/or hemorrhage and damage to the structural integrity of the white line and/or sole is an invitation to infection. Most frequently the infection involves the nonkeratinized layers of the epidermis and the dermis. The resulting accumulation of exudates causes pain and further separation of the hoof capsule from the underlying soft tissues. Drainage may occur at the coronary band, through the white line, or through the sole, but the separation of the hoof capsule may be extensive. If the wall is sufficiently unstable, movement of the wall of the hoof capsule against the underlying soft tissues may cause severe chafing and loss of germinal epithelium. If sufficient damage occurs, infection spreads to the distal phalanx. Contraction of the hoof capsule may be secondary to the pain or to certain shoeing practices used to treat the disease (i.e., placement of the nails in the palmar half of the foot and elevation of the heels). Contraction of the flexor apparatus is also likely a sequela to chronic pain.

The exact causes of pain in chronically laminitic horses are undetermined but are likely to be related to continued ischemia, inflammation, and trauma to the dorsal lamellae, and ischemia or inflammation associated with bruising of the soft tissues of the sole immediately distal to the solar margin of the distal phalanx. Pain is also associated with foci of infection causing increased subsolar or intramural pressure. Additionally, contraction of the hoof may cause pain localized to the palmar aspect of the foot.

PRESENTATION, DIAGNOSIS, AND EVALUATION

The diagnosis of chronic laminitis is seldom a challenge because the gait and appearance are characteristic, and radiographs usually remove all doubt. Occasionally nerve blocks are necessary to localize the pain to the foot in mildly affected horses, and these results are interpreted in conjunction with hoof tester application and radiographs.

Chronic laminitis in horses can manifest in one of the following ways:

1. As the continuation of acute laminitis
2. As the recurrence of past chronic laminitis
3. With an unknown history because the acute phase was never observed or the horse was purchased without knowledge of the disease

Full evaluation of the history, the horse, and the digits are all important to determine the prognosis and treat-

ment. The severity of the initial acute phase is the best indicator of the extent of the original damage and thus is a major factor in the prognosis. The duration of the disease since the acute phase gives some indication as to how much lamellar repair process may have stabilized the distal phalanx within the hoof capsule. The severity of the horse's lameness (e.g., how willing it is to walk, how stiffly it walks, how willing it is to pick up a foot, and how much it lies down) do not correlate as well with the prognosis as they do in acute laminitis, and they do not necessarily correlate with the clinical appearance of the foot or the radiographic changes. How the animal preferentially places its foot may indicate the distribution of lamellar injury; for example, a horse that preferentially bears weight on its heels reduces the tension in the dorsal lamellae and the compression of the sole beneath the dorsal margin of the distal phalanx. Similarly, a horse that lands on one side of its foot may be protecting the contralateral wall or sole. Additionally, the way a horse moves is an adjunct to determining the placement and type of shoe to use. Observation of the hoof wall, sole, and white line, and palpation of the coronary band are clinical indicators of the pathology that has occurred within the digit (e.g., capsular distortion, displacement of the distal phalanx, the presence of infection, and secondary contraction of the hoof or flexor apparatus).

RADIOGRAPHIC FINDINGS

From the perspective of diagnosis, the radiographic features of chronic laminitis are well documented. To assist in the prognosis and treatment, several observations are valuable. High-quality lateral, dorsopalmar, and dorsopalmar oblique projections are required. The exposure must allow good visualization of the hoof capsule. Radiopaque markers are invaluable to determine the position of the distal phalanx in relation to surface landmarks. For the lateral radiograph a linear marker should be placed on the midsagittal dorsal hoof wall starting at the coronary band and extending distally, and a point marker should be placed at the true apex of the frog. Additionally, for the dorsopalmar radiograph, linear markers may be placed on the medial and lateral walls of the hoof capsule.

The lateral radiograph should be examined to determine the thickness of the dorsal hoof wall, the degree of capsular rotation, the angle of the solar surface of the distal phalanx to the ground, and the distance between the dorsal margin of the distal phalanx and the ground. The dorsopalmar view is most useful to determine whether mediolateral rotation of the distal phalanx within the hoof capsule or mediolateral imbalance are present. The location of gas pockets is determined by correlating the findings of the lateral and dorsopalmar radiographs. The margin of the distal phalanx is evaluated for pedal osteitis, sequestra, and margin fractures on the oblique dorsopalmar view.

Positive contrast venography of the foot may indicate the presence of filling defects in the digital vasculature (the lamellar vessels, the circumflex area, and the terminal arch) that signify a poor prognosis. It is important that the venogram is performed with a good tourniquet and the contrast medium infused while the foot is unloaded to prevent artifactual filling defects.

OUTCOME AND PROGNOSIS

The eventual outcome of treatment for horses with chronic laminitis can be divided into function and morphology. The functional outcome is most likely to dictate the difference between athletic activities, pasture soundness and euthanasia. The morphologic outcome is more likely to determine the degree to which continued and potentially lifelong corrective measures are necessary. Although fair correlation exists between the functional and morphologic outcomes, some horses with seemingly modest morphologic changes are euthanized, whereas others go on to perform more strenuous athletic activity than the morphologic appearance would lead one to expect.

At the onset of chronic laminitis the eventual outcome is hard to predict, but the most important indicator for survival remains the severity of the initial insult. The appearance of the initial radiographs does not necessarily correlate with either functional or morphologic outcome. However, the thickness of the sole and the angle between the solar surface of the distal phalanx and the ground are fair indicators of the difficulty of treatment, and both are more useful than the degree of capsular rotation. The thickness of the soft tissues dorsal to the parietal surface of the distal phalanx suggests the prognosis in horses with distal displacement of the distal phalanx in that it indicates the severity of the original injury. In horses with capsular rotation, the eventual morphologic outcome only becomes apparent as the new dorsal hoof grows down through the middle third of the wall.

TREATMENT

The ultimately desired outcome of treatment of horses with laminitis is freedom from pain and feet that look and function normally. Obviously major limitations exist to achieving these ideals. The treatment of chronic laminitis is multifaceted and includes supportive care of the feet, medical therapy, surgical intervention, and nutritional management. In contrast to treating horses with acute laminitis, for which medical therapy frequently assumes priority, supportive therapy is the most important element for success in the treatment of horses with chronic laminitis.

Supportive Therapy

It is not possible to directly reattach the mechanically separated lamellae. Instead the return of the mechanical function of the wall is a gradual process that may take as long as 9 months in the absence of complications. Supportive therapy maintains an environment that enhances natural healing and/or the efficacy of other therapy. In the case of chronic laminitis, this therapy is rest and hoof care. Absolute stall rest in acute and early stages of chronic laminitis is imperative because movement of the horse is associated with increased stress within the damaged lamellae. Later on, the need for rest must be balanced against the need to restore normal function of the hoof capsule that comes with repeated expansion and contraction of the capsule as the animal moves.

The mainstay of hoof care is therapeutic shoeing. In considering hoof care in horses with chronic laminitis, the following three goals for therapy are present:

1. To stabilize the distal phalanx within the hoof capsule
2. To control pain
3. To encourage new hoof growth to assume the most normal relationship to the distal phalanx possible

The hoof must be stabilized so that no further injury is sustained by the remaining lamellar attachments or the new lamellar attachments while they are formed. It is desirable to control the horse's pain for humanitarian reasons as well as to restore limited function as the affected foot/feet heal to spare the other limbs from excessive weight bearing. Encouragement of the foot to return to normal form, both in appearance and anatomically, is the surest way to optimize future function.

To achieve each of these goals several principles or objectives must be considered. These objectives cannot be completely categorized according to goal, because the goals are at least in part interdependent, and a given objective may partially satisfy more than one goal. For example, an increase in stability helps decrease pain because instability is in part the cause of pain. Although instability and pain within the foot are both of immediate concern in the treatment of laminitis, restoration of the normal relationship between the distal phalanx and the hoof capsule is initially a secondary consideration. Restoration of the normal relationship between the distal phalanx and the hoof capsule becomes more important when instability and pain are controlled and the new hoof wall grows out.

Stabilizing the hoof capsule requires decreasing the stress on the most damaged lamellae. Therefore the objectives are to reduce the load on the most severely affected wall, transfer load to the less severely affected wall, transfer load to the ground surface of the foot, and decrease the moment around the distal interphalangeal joint as necessary. Pain caused by lamellar stress and injury is in part controlled by increased stability within the foot. Pain associated with subsolar ischemia, trauma, and bruising can be reduced by avoiding direct pressure on the ground surface of the foot immediately distal to the margin of the distal phalanx. The most important principle in limiting the residual capsular rotation while the hoof initially grows out is to eliminate load on the distal dorsal wall. Later, when there is concavity to the dorsal hoof wall, more direct intervention may be needed. A limited although steadily increasing number of tools are available to the veterinarian and farrier to apply these principles, but the permutations in which they may be applied is far greater.

The starting point of supportive therapy varies greatly with clinical severity, pattern of distal phalangeal displacement, and prior duration of the disease. As such, each horse must be treated as an individual. Therefore no one technique will be satisfactory in each case. This does not mean that the clinician must maintain a battery of techniques for specific situations, but rather that he or she should understand how flexible application of different techniques can satisfy different circumstances. Above all,

the focus should be maintained on principles and not methods. The three different types of distal phalangeal displacement mentioned here warrant separate discussion.

Dorsal Capsular Rotation

The treatment of dorsal capsular rotation consists of several stages. Initially, supportive therapy started in the acute phase of the disease is continued until the horse shows signs of improvement associated with cessation of further displacement. The supportive therapy should acknowledge the principles of stabilization and pain control to include the following steps:

- Removal of shoes already in place that are potentially contributing to instability (i.e., most normal shoes)
- Beveling of the toe
- Application of high-density Styrofoam to the ground surface of the foot or a Redden Modified Ultimate (Advance Equine, Versailles, Ky.), a combination of a cuff and wedge pads, in conjunction with silicone putty to fill the concavity of the sole

After 3 to 6 weeks, the horse can usually be shod.

The first shoeing is critical to future success. It is the most time-consuming part of the treatment but will save time later and reduce the likelihood of complications. The technique for shoeing the laminitic horse with a shoe and wedge rails manufactured by the Equine Digital Support System (EDSS; Penrose, Colo.) or custom-forged aluminum four-point rail shoes (Figure 10.7-1)—discussed in the following text—is that which this author uses most frequently. Alternatives to this method are discussed later in the chapter.

With the previously mentioned method, the foot may be blocked with local anesthetic; it must be trimmed and the shoe sized and positioned relative to the underlying distal phalanx regardless of the conformation of the hoof. Therefore measurements must be made from radiographs taken before shoeing as a guide. Better still are repeat radiographs at each stage of shoeing. First a line (Figure 10.7-2, *Line 1*) is drawn on a lateral radiograph parallel and approximately 15 mm (a normal sole thickness) distal to the solar surface of the distal phalanx; this line may extend distal to the wall and sole in the dorsal half of the foot. A second line (Figure 10.7-2, *Line 2*) is drawn parallel and approximately 15 to 18 mm (normal dorsal wall thickness) dorsal to the parietal surface of the distal phalanx. The point at which line 1 intersects line 2 is noted (Figure 10.7-2, *Point A*). A third line is drawn from the dorsal margin of the distal phalanx distally and perpendicular to line 1 until it intersects line 1 (Figure 10.7-2, *Point B*).

The wall and sole are trimmed parallel to coincide with line 1 (Figure 10.7-3, A and B). Depending on the degree of capsular rotation and the length of the hoof wall, it may be impossible to trim the wall and sole from toe to heel parallel to the solar border of the distal phalanx without trimming the sole in the dorsal half of the foot too thin. It is imperative to maintain the maximal sole thickness at a normal level. Therefore to preserve the thickness of sole, the foot is trimmed from the heels dorsally to the point where trimming would encroach on the normal thickness of sole. The result is that toward the palmar sur-



Figure 10.7-1 A four-point rail shoe.

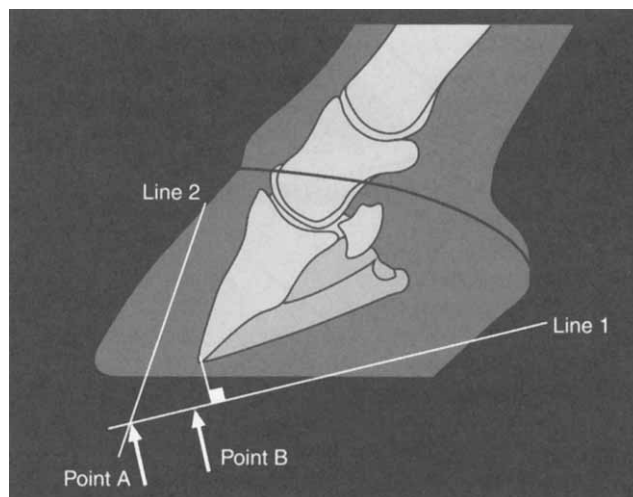


Figure 10.7-2 A schematic representation of a lateral radiograph of a foot with dorsal capsular rotation. Line 1 is drawn approximately parallel and about 15 mm distal to the solar surface of the distal phalanx. Line 2 is drawn parallel and approximately 15 to 18 mm dorsal to the parietal surface of the distal phalanx. Point A at the intersection of line 1 and line 2 is the furthest dorsal point the toe of the shoe should be set. Point B is approximately 6 mm dorsal to the dorsal margin of the distal phalanx and is the approximate location of the point of breakover.

face the wall may be trimmed to a different angle in relation to the distal phalanx than it is dorsally so that a shoe cannot be stably set on the foot. Lowering the heels in this manner also increases the tension in the deep digital flexor tendon.

The shoe is sized so that the toe of the shoe does not extend beyond point A and the heels of the shoe extend 6 to 8 mm palmar to the heels (Figure 10.7-3, C). The toe of the EDSS shoe or an equivalent shoe is aggressively squared off and rolled and positioned so that the breakover point is approximately 6 mm dorsal to point B (some clinicians prefer to set the breakover point even further towards the palmar surface); this is determined by ref-

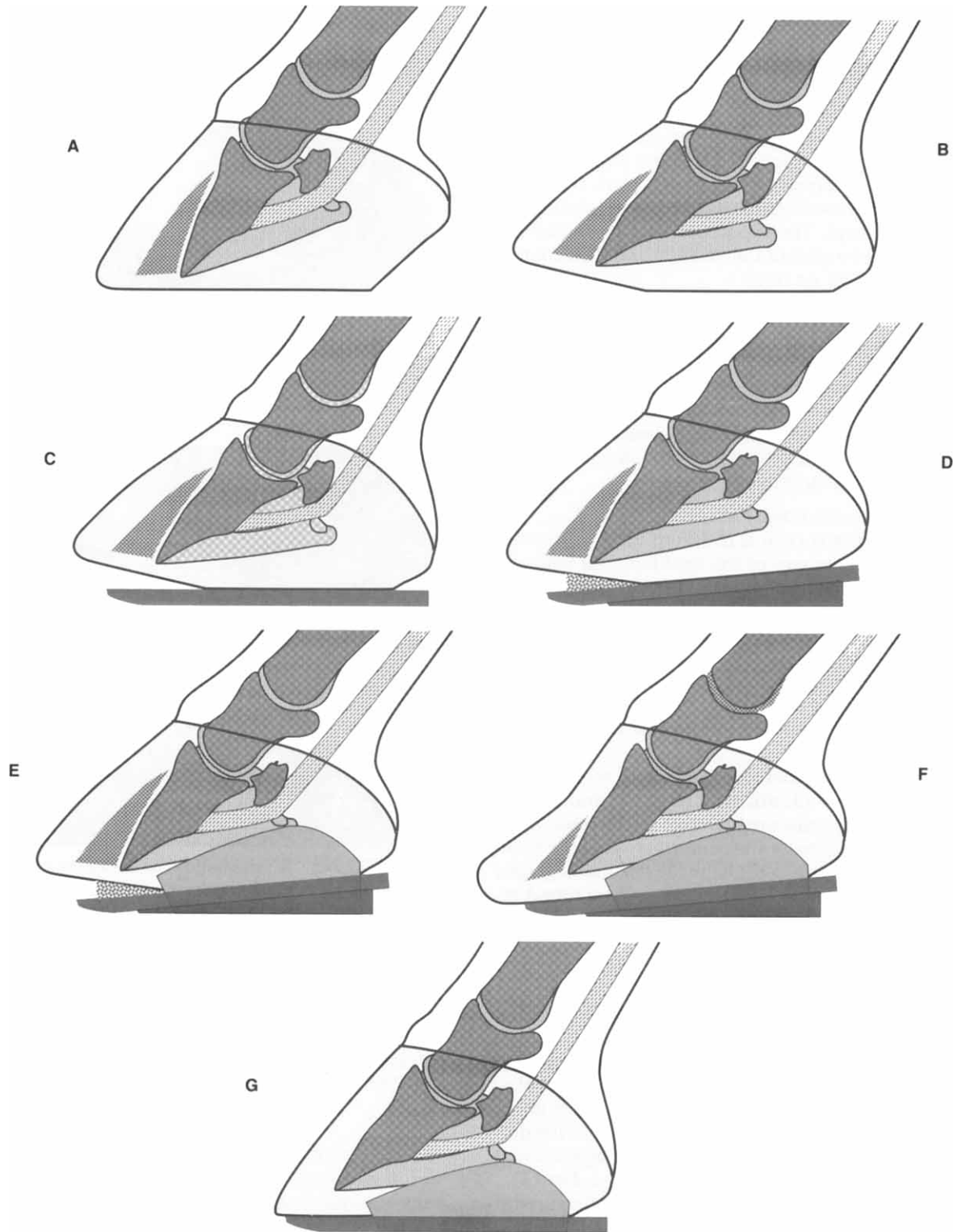


Figure 10.7-3 Technique for application of a four-point shoe to the hoof of a horse with chronic laminitis. **A**, A schematic diagram of a horse's foot with chronic laminitis that has recently developed capsular rotation (dorsal). **B**, After trimming along line 1 in Figure 10.7-2. **C**, Position of the shoe in relation to the distal phalanx. **D**, After the dorsal quarters are built up with a composite to allow attachment of the rail shoe. **E**, Silicone putty is packed into the concavity of the palmar aspect of the ground surface of the foot and space between the branches of the shoe. **F**, After some months with optimal healing the new dorsal wall grows approximately parallel to the parietal surface of the distal phalanx. **G**, After the rails have been removed but the silicone putty is still in place.

erence to the apex of the frog or confirmed with radiographs. If the ground surface of the foot is not level because the dorsal half of the foot could not be trimmed without unduly decreasing sole thickness, a triangular-shaped gap is present between the wall and shoe dorsally when the shoe is set flat on the palmar aspect of the foot (i.e., parallel to the solar margin of the distal phalanx). This gap must be filled so that the shoe fits the ground surface of the foot; the clinician can achieve this aim either by building up the ground surface of the foot with a synthetic polymer such as Equilox (Equilox International, Pine Island, Minn.) or by attaching reverse wedge shims to the dorsal part of the shoe. The shoe is then nailed to the foot, usually with two to three nails in the quarter of each branch, but the nail points are not wrung. If the shoe is correctly placed, a gap between the toe of the shoe and the adjacent wall and sole will be present. This gap will ensure there is no pressure distal to the dorsal margin of the distal phalanx. A lateral radiograph is useful to confirm the position of the shoe in relation to the distal phalanx. If it appears that the shoe could be better positioned, the shoe is removed and reattached and the radiograph repeated. Once the position of the shoe is satisfactory, the nail points are wrung and the nails clinched.

To compensate for the increase in tension in the deep digital flexor tendon caused by the lowering of the heels of the hoof capsule, the heels of the shoe are raised by the application of wedge-shaped rails to the axial ground surface of each branch (Figure 10.7-3, D). In the case of the EDSS shoe, the rails are bolted in place. In the case of a hand-forged shoe, they are welded in place. The heels of the hoof should be lowered and the heels of the shoe should be raised. Raising the heels is preferable to leaving the heels of the hoof long because the former method moves the ground surface of the hoof that can bear weight in a more palmar direction. The height of the rails at the heels is such that the ground surface of the foot is usually at 4 to 6 degrees to the ground, but ideally the height of the heels should permit the foot to land flat or with the heel slightly first. The advantage of the bolted on rails over the forged on rails is that the former can be changed after the shoe is applied. The rails are positioned axially on the branch of the shoe so that the horse can break over medially and laterally with greater ease.

To enable the palmar 50% to 70% of the ground surface of the foot between the branches of the shoe to bear weight, the concavity of the sole and the sulci of the frog and the space between the branches of the shoe are filled with either a silicone putty (Figure 10.7-3, E) or equivalent. The silicone putty is held in place by a mesh that is inserted between the shoe and the foot when the shoe is nailed to the foot so that the putty is distributed on both sides of the mesh.

The foot should be trimmed and the shoe and sole support reset every 4 to 6 weeks. If the lamellae are healing optimally, the new hoof wall should grow almost parallel to the parietal surface of the distal phalanx (Figure 10.7-3, F). As the distal phalanx becomes more stable within the hoof capsule, it should be possible to gradually reduce the height of the heels. After 4 to 6 months, sufficient stability should be restored to permit the horse to be shod with a shoe and sole support without heel el-

evation (Figure 10.7-3, G). After 6 to 8 months, the sole support may be removed. After 8 to 12 months it may be possible to revert to routine shoeing or allow the horse to go barefoot.

This technique has several complications. The quality of the horn may deteriorate with prolonged application of acrylics to build up the wall. The walls at the quarters become thin and weaker with time if they are the primary weight-bearing structures. The heels of the hoof capsule contract when the heels are elevated. Therefore the measures used to treat laminitic horses are a compromise, and the pattern of shoeing should be returned to normal as soon as possible.

Alternative Methods of Shoeing Horses with Capsular Rotation

Several alternative techniques exist that follow the same or similar principles but use different types of shoe, different ways to recruit the ground surface of the foot to bear weight, and different ways to elevate the heels. Instead of an open-heeled shoe, an egg bar shoe or reverse shoe may be used. The toe of an egg bar shoe should be modified as previously described; the bar acts as a short extension. With a reverse shoe, no toe treatment is required and the most palmar aspect of the shoe acts as the bar of an egg bar shoe. As with the regular shoe, the need for ground surface support and heel elevation must not be ignored.

As an alternative to rails, wedge pads or shims inserted between the shoe and the foot can be used to elevate the heels. However, this method does not permit the same ease of mediolateral breakover that a rail shoe does. Additionally, it is harder to change the height of heel elevation when pads are used because the shoe must be removed.

Several other methods exist to recruit part or the entire ground surface of the foot to bear weight. Quick-setting urethane (Equi-Thane and Equi-Pak, Vettec, Oxnard, Calif.) can be poured into the concavity of the sole and the space between the branches of the shoe. The urethane is available in formulations that set with different degrees of hardness. Caution must be used when packing the sole of the foot with hard compounds in case they increase the pressure on the subsolar epidermis and dermis and compromise the solar blood supply. Alternatively, pads applied between the foot and the shoe distribute weight across the ground surface of the foot. It is important that weight is transferred from the ground to the pad across the space between the branches of the shoe or the pad may simply displace distally into the space and fail to support the foot. Some pads are formed so that part of the pad fills the space (e.g., a heart bar pad). Alternatively, another pad must be attached to the distal surface of the primary pad to fill the space; this technique is used in the EDSS. Pads are invariably used with some type of packing material between the sole and the solar surface of the pad. The heart bar of a heart bar shoe provides support to the ground surface of the foot through the frog and works well when skillfully applied to the right horses. Although usually used alone, the heart-bar shoe can be used in conjunction with a pad or silicone putty.

Alternatively, if the horse is too sore to permit nailing the shoe to the foot, the shoe may be glued on. Various

proprietary shoes are designed to treat laminitic horses that incorporate heel elevation or a heart bar that can be glued in place with plastic tabs or cuffs. Alternatively, a shoe that would otherwise be attached with nails can be glued to the foot. The shoe can be attached directly to the hoof wall with acrylic interposed between the shoe and the foot and the support added later. Or the shoe and sole support can be held in place while strips of fiberglass coated with acrylic are applied from one wall to the other to cover both shoe and sole support.

Distal Displacement of the Distal Phalanx

The essential difference between the treatment of a horse that shows distal displacement of the distal phalanx and a horse that primarily shows capsular rotation is that neutralizing the moment around the distal interphalangeal joint is less important in the former. As with capsular rotation, the initial therapy is a continuation of acute supportive therapy. This therapy consists of the clinician's packing the ground surface of the foot with silicone putty or the equivalent, taping Styrofoam to the ground surface of the foot, or keeping the horse on sand. However, in horses with distal displacement, this author may continue the therapy for considerably longer, 2 to 4 months if necessary, before shoeing the horse. The shoes are similarly squared off, rolled, and fitted as previously described. The heels are seldom elevated. The solar cavity, the sulci of the frog, and the space between the branches of the shoe are similarly filled with silicone putty. After 4 to 8 months the sole support can be removed. After 8 to 12 months it should be possible to revert to routine shoeing or allow the horse to go barefoot.

Mediolateral Rotation of the Distal Phalanx

Less is known about treating horses with mediolateral rotation of the distal phalanx—a condition much less common than dorsal capsular rotation or distal displacement. Theoretically the hoof capsule can be stabilized in relation to the distal phalanx by reduction of weight bearing on the affected side by an increase in weight bearing on the contralateral side. The clinician could accomplish this goal by either increasing the thickness of the branch on the contralateral side or by extending the shoe on the contralateral side as a lever. This author has had success in controlling mediolateral rotation in a limited number of horses by applying the rail shoe in combination with silicone putty and setting the shoe wide on the unaffected side. Although this has visibly improved comfort and/or abolished the evidence of mediolateral rotation over time, it has not necessarily translated into greater survival of the horses—the complication rate with this condition appears to be high and more experience with the technique is necessary.

Medical Treatment and Nutritional Management

In the early stages of chronic laminitis, medical therapy initiated in the acute phase is continued and then tapered off during a period of 1 to 2 weeks. After this period, treatment with phenylbutazone is continued to control pain and inflammation as necessary. A balance must be struck

between providing relief from pain and the gastrointestinal side effects of nonsteroidal antiinflammatory drugs.

No systematic guidelines exist concerning the use of systemic antibiotics in the treatment of chronic laminitis. However, use of these drugs may be warranted in horses in which cavitation between the hoof capsule and the distal phalanx is suspected and the structure of the sole or white line is weakened, predisposing the horse to develop infection beneath the hoof capsule. This author also uses systemic antibiotics in conjunction with surgical drainage after the infection of the subcapsular soft tissues has been definitively established, usually for 10 to 20 days. Longer therapy is justified in the presence of osteomyelitis of the distal phalanx. Topical antibiotics may be flushed into subcapsular cavities through the drainage sites, topically applied under dressings, or packed into the wound as methylmethacrylate impregnated beads. The use of intravenous (IV) perfusion of the limb with antibiotics is well established for the treatment of distal limb musculoskeletal infections, and although its efficacy may be limited in horses with chronic laminitis because of reduced vascularity of the tissues, this treatment deserves consideration.

IV perfusion of the distal limb with radiographic contrast medium is said to decrease lameness and increase hoof growth within a few days of the study and the effect lasts as long as several weeks. The potential mechanisms by which this might occur include mechanical removal of thrombi or erythrocyte aggregates, decreased platelet aggregation, a vasoactive response that causes dilation or reduced constriction, or an osmotic effect that decreases lamellar edema. This concept is intriguing, but further clinical experience is needed to fully evaluate the effectiveness of this technique.

Horses in which the presence of Cushing's syndrome is established should be treated with pergolide or cyproheptadine, a concept discussed in Chapter 15.3. Failure to do so is associated with recurrent exacerbation of the disease. The use of thyroid hormone replacement or supplementation is of questionable benefit. Thyroid hormone replacement may simply encourage weight loss in obese horses.

No good guidelines exist on the nutritional management of horses with chronic laminitis. To limit the weight borne by each front foot it is advisable that obese horses lose weight and that excessive weight gain be prevented. The practice of starving horses with chronic laminitis is contraindicated because an adequate plane of nutrition is required to encourage optimal healing; diets deficient in protein or calcium are associated with poor hoof growth and quality. Therefore the nutritional management of laminitis requires balance. A good quality grass hay or alfalfa is recommended, and biotin supplementation is known to increase the strength of the hoof wall.

Surgical Treatment

Deep Digital Flexor Tenotomy

Deep digital flexor tenotomy is primarily indicated in three instances. First, it is indicated for horses that show progressive rotation of the distal phalanx despite more conservative efforts at stabilization. This particularly ap-

plies to horses in which the distal phalanx is already penetrating the sole of the foot. Second, it is indicated for horses with persistent severe discomfort that show little to no growth of the sole or dorsal hoof wall despite apparent radiographic evidence of stability of the distal phalanx. After deep digital flexor tenotomy a dramatic increase in the rate of sole growth and decreased pain frequently occurs. Although a deep digital flexor tenotomy is considered a salvage procedure, some horses return to limited athletic performance. Last, deep digital flexor tenotomy is believed to correct severe secondary flexural deformities that develop during the later stages of treatment.

The deep digital flexor can be divided in the midmetacarpal region or at the midpastern. Deep digital flexor tenotomy in the midmetacarpus is easier to perform. Additionally, there appear to be enough soft tissue attachments to the deep digital flexor tendon distal to the tenotomy and proximal to the digital sheath that the distal interphalangeal joint is slightly more stable after a tenotomy in the midmetacarpal region than in the midpastern region. Therefore the clinician has slightly more leeway in selecting the time of application of the shoe if the tendon is cut in the midmetacarpus than if it is cut in the midpastern. Furthermore, if a second tenotomy is necessary, the adhesions associated with the first tenotomy are proximal to the site of the second if midmetacarpal tenotomy is performed first. If the procedures were performed in the other sequence, the adhesions in the pastern could potentially interfere with the effectiveness of a midmetacarpal tenotomy.

Tenotomy in the midpastern can be performed in the standing horse with sedation and local anesthesia, or with the horse under general anesthesia. Surgery performed on a standing horse is quicker and cheaper. Sterility of the surgical site is more easily maintained when surgery is performed with the horse under anesthesia, but the disadvantage is the theoretical risk of hyperextension of the distal interphalangeal joint when the horse recovers from anesthesia. The clinician can limit this risk by recovering the horse in a splint that immobilizes the foot as well as the distal limb, such as a Kimsey splint, or in a cast or cast bandage.

After deep digital flexor tenotomy the toe of the foot is prone to lift as the animal rocks back on its heels or as it walks. This tendency can be countered by relatively short heel extensions. Of greater concern is the tendency of the distal interphalangeal joint to subluxate secondary to lack of support of the navicular bone by the deep digital flexor tendon. In addition to heel extension, heel elevation may further aid in countering the tendency of the distal interphalangeal joint to subluxate.

Drainage and Debridement of the Distal Phalanx

Surgical drainage of purulent exudate from cavities created by separation of the wall or sole from underlying soft tissues is important to reduce the pressure of the fluid. This reduction in pressure alleviates pain and prevents further separation by the expansion of the cavity and enhances the healing process. The optimal location for drainage is at the distal dorsal hoof wall where the plane of the solar epidermal/dermal junction meets the termi-

nal lamellae; drainage from this location will preserve the full thickness of the sole. The difficulty is in deciding when to provide drainage. Premature drainage may contaminate a sterile cavity, and delayed drainage is likely to increase lamellar or subsolar separation. Drainage of sterile cavities has been advocated to relieve pressure; in a normal horse fenestration of the dorsal hoof wall presents little risk of infection. However, in a horse with vascular compromise of the dermal lamellae the risk of infection would be enhanced. Therefore this author avoids opening sterile cavities.

Debridement of the distal phalanx is problematic for two reasons. First, it can be difficult for the clinician to confirm that osteomyelitis is present. Perforation of the sole does not itself imply that there is osteomyelitis, and it is hard to radiographically differentiate lysis of the distal phalanx because of infection from lysis caused by aseptic inflammation. Exposure and debridement of a distal phalanx that is not septic may permit infection to become established. Second, the benefits of debridement are questionable. Undoubtedly some horses exist in which debridement encourages resolution of the infection when performed in conjunction with other appropriate medical therapy. However, in other horses the debridement simply exposes deeper bone to the source of infection so that the distal phalanx is progressively destroyed.

When separation of the hoof capsule from the underlying tissues causes chafing at the coronary band, the proximal wall can be resected to protect the germinal epithelium. It is best to taper the resection in a proximal to distal direction to spread out the pressure and minimize the likelihood of creating another ridge of pressure further distally.

Grooving and Hoof Wall Resection

Continued divergence of the dorsal hoof wall away from the parietal surface of the distal phalanx after the distal wall has been relieved of weight bearing may respond to coronary band grooving or dorsal hoof wall resection. Coronary band grooving mechanically dissociates the new proximal wall from the older distal wall. Additionally, it enhances hoof growth by the coronary band proximal to the groove by some mechanism secondary to reducing pressure at the coronary band. The groove grows out as the new wall migrates distally.

Resection of the dorsal hoof wall may be partial or complete. A complete hoof wall resection removes the entire wall from the weight-bearing surface to the coronary band. A partial resection extends a variable distance proximally from the weight-bearing surface. Therefore rather than dissociating the proximal and distal hoof wall, the distal wall is simply removed. This approach does allow debridement of the more superficial hyperplastic epidermis. However, the remaining lamellar attachments to the dorsal hoof wall are now functionless, and the tendency of the dorsal margin of the distal phalanx to impinge on the soft tissues of the immediately adjacent sole is potentially increased. Also, stress is now concentrated in the hoof wall at the margins of the resection increasing the tendency for separation within the hoof wall at these points. This is compounded by the lack of the tension band that the dorsal hoof wall provides between the quar-

ters. For these reasons, the dorsal hoof wall is resected less frequently now than in the past.

Unfortunately, neither technique is likely to improve deformity in the dorsal hoof wall secondary to changes in the shape of the coronary groove or to redirect of the coronary band dermal papillae. Also if the basal layers of the epithelium are displaced away from the parietal surface of the distal phalanx by thickening of the underlying dermis, it is not possible for the epidermis to realign with the distal phalanx. To date, no technique has been described to remove the dermal component of the lamellar wedge that fills the space created by capsular rotation.

Other auxiliary techniques include the use of casts, external fixation, or transfixation pin casts to bypass the weight-bearing function of the foot. A detailed discussion of these techniques is beyond the scope of this chapter. However, the use of casts precludes inspection of the limb and treatment of any secondary infection.

TREATMENT FAILURE

Many reasons exist for the failure of treatment in laminitic horses. The overwhelming severity of the initial disease is the most important, particularly when persistent infection develops. Also, financial constraints are important because the treatment can be very long, tiring, and expensive. Therefore many owners stop treatment when the full im-

plications of the cost or the psychologic or physical toll of nursing care become apparent.

Failure of owners to comply with recommendations is not uncommon. When the treatment progresses, the horse's lameness diminished before full mechanical recovery is achieved. Owners are sometimes tempted to liberally interpret recommendations for rest, and the ensuing excessive exercise precipitates more lamellar injury, which leads to a setback in the condition. Also, failure to maintain regular appointments with veterinarian and farrier leads to overgrowth and/or distortion of the hoof capsule and poor positioning of the shoe, both of which prolong the treatment and increase the likelihood of treatment failure.

Supplemental Readings

Curtis S, Ferguson DW, Luikart R et al: Trimming and shoeing the chronically effected horse. *Vet Clin North Am Equine Pract* 1999; 15:463-480.

Redden RF: Shoeing the laminitic horse. *Proceedings of the 43rd Annual Meeting of the American Association of Equine Practitioners*, pp 356-359, 1997.

Redden RF: *Understanding Laminitis*, pp 46-103, Lexington, Ky, The Blood-Horse, 1998.

CHAPTER 10.8

Shoeing Management of Sheared Heels

STEPHEN E. O'GRADY
The Plains, Virginia

Sheared heels can be defined as a hoof capsule distortion that results from displacement of one heel bulb proximally relative to the adjacent heel bulb (Figure 10.8-1). When the weight of the horse is not distributed uniformly over the entire hoof during the landing phase of the stride, one focal area of the foot, usually the heel or heel and accompanying quarter, receives a disproportionate amount of the total force of impact. The resultant force leads to a structural breakdown between the heel bulbs. The degree of deformity in the affected heel depends on the amount of impact sustained by the individual foot. The clinician diagnoses sheared heels by a disparity between the medial and lateral heel lengths of 0.5 cm or more. Lameness has been attributed to this condition, but a number of sound horses also have distorted hoof capsules.

Of equal importance is the fact that this continual disproportionate impact and increased compressive stresses on one heel predisposes the foot to pain, corns, subsolar bruising, pedal osteitis, quarter and heel cracks, fracture of the bar, deep fissures within the base of the frog, and thrush in narrow frogs. In fact, seldom is one of the above conditions present when not accompanied by a sheared, contracted, or under-run heel. The management of sheared heels is through appropriate trimming and shoeing aimed at restoration of proper heel alignment. Sheared heels can occur in the hind feet as well as the forefeet (Figure 10.8-2).

STRUCTURAL CHANGES TO THE FOOT

The equine hoof capsule is a viscoelastic structure that has the unique ability to deform when weight is accepted uni-

ters. For these reasons, the dorsal hoof wall is resected less frequently now than in the past.

Unfortunately, neither technique is likely to improve deformity in the dorsal hoof wall secondary to changes in the shape of the coronary groove or to redirect of the coronary band dermal papillae. Also if the basal layers of the epithelium are displaced away from the parietal surface of the distal phalanx by thickening of the underlying dermis, it is not possible for the epidermis to realign with the distal phalanx. To date, no technique has been described to remove the dermal component of the lamellar wedge that fills the space created by capsular rotation.

Other auxiliary techniques include the use of casts, external fixation, or transfixation pin casts to bypass the weight-bearing function of the foot. A detailed discussion of these techniques is beyond the scope of this chapter. However, the use of casts precludes inspection of the limb and treatment of any secondary infection.

TREATMENT FAILURE

Many reasons exist for the failure of treatment in laminitic horses. The overwhelming severity of the initial disease is the most important, particularly when persistent infection develops. Also, financial constraints are important because the treatment can be very long, tiring, and expensive. Therefore many owners stop treatment when the full im-

plications of the cost or the psychologic or physical toll of nursing care become apparent.

Failure of owners to comply with recommendations is not uncommon. When the treatment progresses, the horse's lameness diminished before full mechanical recovery is achieved. Owners are sometimes tempted to liberally interpret recommendations for rest, and the ensuing excessive exercise precipitates more lamellar injury, which leads to a setback in the condition. Also, failure to maintain regular appointments with veterinarian and farrier leads to overgrowth and/or distortion of the hoof capsule and poor positioning of the shoe, both of which prolong the treatment and increase the likelihood of treatment failure.

Supplemental Readings

Curtis S, Ferguson DW, Luikart R et al: Trimming and shoeing the chronically effected horse. *Vet Clin North Am Equine Pract* 1999; 15:463-480.

Redden RF: Shoeing the laminitic horse. *Proceedings of the 43rd Annual Meeting of the American Association of Equine Practitioners*, pp 356-359, 1997.

Redden RF: *Understanding Laminitis*, pp 46-103, Lexington, Ky, The Blood-Horse, 1998.

CHAPTER 10.8

Shoeing Management of Sheared Heels

STEPHEN E. O'GRADY
The Plains, Virginia

Sheared heels can be defined as a hoof capsule distortion that results from displacement of one heel bulb proximally relative to the adjacent heel bulb (Figure 10.8-1). When the weight of the horse is not distributed uniformly over the entire hoof during the landing phase of the stride, one focal area of the foot, usually the heel or heel and accompanying quarter, receives a disproportionate amount of the total force of impact. The resultant force leads to a structural breakdown between the heel bulbs. The degree of deformity in the affected heel depends on the amount of impact sustained by the individual foot. The clinician diagnoses sheared heels by a disparity between the medial and lateral heel lengths of 0.5 cm or more. Lameness has been attributed to this condition, but a number of sound horses also have distorted hoof capsules.

Of equal importance is the fact that this continual disproportionate impact and increased compressive stresses on one heel predisposes the foot to pain, corns, subsolar bruising, pedal osteitis, quarter and heel cracks, fracture of the bar, deep fissures within the base of the frog, and thrush in narrow frogs. In fact, seldom is one of the above conditions present when not accompanied by a sheared, contracted, or under-run heel. The management of sheared heels is through appropriate trimming and shoeing aimed at restoration of proper heel alignment. Sheared heels can occur in the hind feet as well as the forefeet (Figure 10.8-2).

STRUCTURAL CHANGES TO THE FOOT

The equine hoof capsule is a viscoelastic structure that has the unique ability to deform when weight is accepted uni-



Figure 10.8-1 Palmar view of a sheared heel. Note the disparity between the medial and lateral heel lengths; also note that the coronary band bulges abaxially to create a lip.



Figure 10.8-2 Plantar view of a sheared heel. Note the underrun heel.

formly. However, if the energy of impact is continually placed on one heel, over time structural changes occur. The increased focal impact on one side of the foot causes the hoof wall to assume a steeper angle (i.e., the wall becomes straighter). Along with the increased hoof angle, contracture of the heel subjected to the greater forces will soon follow. This contracture decreases the ground surface of the foot, results in a lack of expansion on that side, and makes the solar surface of the foot asymmetrical. This asymmetry is easily seen if the examiner remembers that the frog normally bisects the hoof.

Over time, the hoof wall begins to “roll under” on the affected side, which further decreases support under that area of the foot. The laminae above the hoof wall on the affected side are subjected to abnormal shearing forces that result in hemorrhage, stretching, or tearing. The side of the foot that first contacts the ground develops a flare caused by bending of the hoof tubules. With the abnor-

mal strike pattern associated with sheared heels, the distal interphalangeal, pastern and fetlock joints are loaded unevenly. In addition to the uneven loading on the joints, a rotational torque is created around the point where the foot first contacts the ground. This torque is transferred up the limb and places undue stress on joints, ligaments, and the suspensory apparatus. This type of landing pattern also places abnormal concussive forces on the navicular bone and its associated ligaments.

ETIOLOGY

To formulate a rational approach to therapeutic shoeing, the etiology of sheared heels must be considered. Sheared heels can be conformational or acquired. Conformational faults in the upper limb that change the flight phase of the stride can result in unequal loading of the foot as it strikes the ground. In this instance, the altered flight pattern causes the horse to contact the ground with one side of the foot before impact on the opposite heel, followed by full weight bearing on that side of the foot. This focal impact drives the heel proximally and creates the unequal heel height. In the conformationally predisposed horse, the carpus is generally rotated laterally but occasionally medially. When viewed from the front, although the entire limb faces outward (or in some instances, medially) the limb from the knee to the ground surface of the foot forms a straight line that indicates a rotational deviation of the limb.

With the knee facing outward, breakover takes place in this direction and changes the flight of the foot during the stride so that the foot is unable to land evenly on both heels. As the horse approaches the landing phase of the stride, this flight pattern forces the foot to contact the ground on one side of the foot and then sustain excessive impact on the opposite side. A slow motion video camera will enable the viewer to distinguish the point where the foot contacts the ground on one side and the point where the hoof impacts the surface on the other side. Furthermore, there appears to be a correlation between an offset third phalanx and sheared heels. Most often the third phalanx is offset laterally within the hoof capsule rather than directly under the first and second phalanges; the ensuing concussive forces cause the medial heel to shear.

Foals may develop a sheared heel at an early age because of a rotational deformity of the forelimbs. Again, this rotational deformity changes the flight portion of the stride causing the foal to land on one side of the foot instead of landing flat.

Improper trimming and shoeing are thought to be the most common cause of sheared heels. This scenario is different from sheared heels that result from rotational deformity because the landing pattern is created by human intervention. Excess hoof wall is removed from one heel, which leads to an abnormal mediolateral orientation of the hoof. Improper or poor trimming may be unintentional because the farrier does not understand the goals of maintaining proper mediolateral orientation or is unable to implement these goals. Because the heels are a different length, a disproportionate force is placed on the longer heel during weight bearing. This force is thought to cause an abnormal shearing force between the heels

and structural breakdown with the affected heel being driven upward.

However, this author used a group of 20 horses (10 broodmares and 10 young riding horses) on a large breeding farm to test the latter hypothesis. All horses landed flat before trimming their feet. One side of the foot was repeatedly lowered, sometimes excessively, but no horse developed sheared heels. With the increased awareness of foot problems by the horse-owning public and with the continued improvement in the quality of horseshoeing, improper trimming of the hoof may not be the main cause of this condition today.

Sheared heels can also arise from attempts to alter conformation by trimming or shoeing. This type of shoeing is performed in an attempt to improve performance, to compensate for faulty conformation, or to deceive a would-be purchaser of a horse. In attempts to correct toe-out conformation, especially in young horses, the owner often lowers the lateral quarter and heel and leaves the medial heel high instead of trimming the foot level. Cosmetic improvement may be evident when the horse stands, but the horse's arc of flight may be changed, leading to an altered landing phase. When trimmed in this manner, the ground surface of the inside of the foot is decreased in length relative to the ground surface of the outside of the foot. When a shoe is then applied, in many instances the branches of the shoe will be unequal in length; this unevenness decreases the foot support and increases the force of impact on the shorter side of the shoe (Figure 10.8-3).

Traction devices such as "stickers" placed on one heel will concentrate the energy of impact to that focal area of the foot. This single heel caulk will cause elevation of one heel, cause the foot to tilt, and change the mediolateral orientation of the foot. Continued use of this type of traction device often leads to proximal displacement of the heel.

DIAGNOSIS

The evaluation of sheared heels begins with visual assessment of hoof and limb conformation with the horse

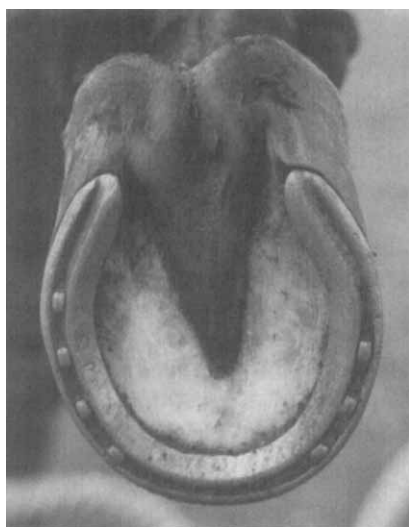


Figure 10.8-3 A shoe that is too small, with unequal branches. Note that the medial heel is displaced proximally.

standing on a hard level surface. The gross changes noted in the foot are proportional to the amount of impact sustained, the extent of structural damage, and the duration of the condition. When sheared heels are present, the heel bulb on the affected side is displaced proximally when the observer is standing behind the horse. When the observer is in front of the horse, the hoof wall on the affected side will be straighter and, in chronic cases, will have begun to roll under the horse.

A marked flare of the hoof wall will be present on the side opposite the affected heel. When viewing from the side of the horse, the observer will see that the coronary band is displaced proximally above the damaged heel instead of having a uniform slope from the toe to the heel. The solar surface of the foot reflects changes elsewhere in the hoof capsule. The foot is less symmetrical and the sole appears wider on the side with the flare and narrower on the side with the underrun wall. A deep fissure is often located at the base of the frog and may extend to the hairline. In more severe cases, when the clinician holds a heel in each hand, he or she will be able to manually move the heels in opposing directions. The horse may show discomfort when this manipulation is performed.

It is important to view the horse in motion on a hard level surface from both the front and rear. The observer should view the horse while it walks and trots. Viewing from behind should enable the observer to determine which part of the foot is contacting the ground and which portion of the foot is receiving the impact. The observer should note the direction of breakover when viewing the horse from the front. Breakover will generally take place to the side of the foot with the affected heel.

If lameness is present and the distorted hoof is thought to be the cause, the pain should be localized to the suspected area with use of hoof testers, diagnostic local anesthesia, and radiology. It should be determined whether the lameness is caused by or related to the sheared heels, or whether another problem exists.

CORRECTIVE SHOEING

Adult Horses

Corrective shoeing coupled with selective trimming of the hoof attempts to decrease the impact on the distorted heel by altering the strike pattern. Hoof trimming should improve the landing pattern of the hoof; trimming the hoof perpendicular to the long axis of the limb does not accomplish this aim because it does not take into consideration any conformational faults. Confusion exists as to which side of the hoof should be lowered. An individual who views an anteroposterior radiograph of a foot with sheared heels will see a narrowing of the proximal and distal interphalangeal joints on the side of hoof elevation and a sliding of the middle phalanx to the lower side. The radiograph will also show that the length of the hoof wall on the side of the sheared heel is longer. These two findings are ample evidence that the hoof wall length should be decreased on the affected side. Clinically, after trimming the heel on the affected side lower, the horse will have a more even (flatter) strike pattern.

This author prefers to trim the foot in stages, each of

which is followed by watching the horse walk on a hard flat surface. Before trimming, the foot is lifted off the ground, the metacarpus is held horizontally and the limb is allowed to hang in its natural position under the horse. The examiner's head is positioned over the foot so as to be able to sight along the limb and down across the solar surface of the foot, evaluating the mediolateral orientation relative to the ground. The affected heel is usually high (longer) when viewed in this manner. The foot is then trimmed level which entails removing more hoof wall on the affected side. The length of the affected heel will then approximate the length of the opposite heel and the end of the heel will be closer to the base of the frog.

No more hoof wall is removed than is required to level the solar surface of the foot. However, additional hoof wall may be removed on the affected side if necessary to achieve the desired strike pattern. Any flares on the opposite side of the foot are removed by rasping the outer hoof wall. A wide web steel straight bar shoe is fitted as symmetrically as possible underneath the long axis of the limb by using the apex of the frog as a central marker. The bar shoe effectively increases the surface area of the foot, provides more expansion (support) on the side with the straighter wall, and stops the vertical movement of the heel bulbs. Wide web aluminum bar shoes can be used if the athletic endeavor of the horse dictates their use. Before the shoe is applied, any remaining hoof wall under the affected heel that can be safely removed is trimmed away. This trimming creates a space between the heel and the shoe that allows the displaced heel to drop down and settle into a more normal configuration (Figure 10.8-4). Several resets with the method described may be needed to achieve (if possible) symmetric heel positions.

Although selective trimming accompanied by some form of rigid support shoe is the treatment of choice, this method does not always change the conformation of the foot if the heel is severely distorted. This author has successfully used another procedure that provides a gross anatomic change in the affected portion of the heel before shoeing. The procedure begins with removal of the shoe. Any excess sole is removed (mild concavity of the sole is created if possible in the case of a flat sole) and the feet are soaked in hot water kept at a constant temperature for 20 minutes. A frog support pad (Lily Pad, Advanced Equine Productions, Versailles, Ky.) is taped to the

bottom of the foot and a heavy cotton bandage is applied to surround the entire foot including the coronary band. The horse is placed in a stall for 24 hours and the bandage is moistened with hot water periodically during that time. Alternatively, following the initial soak the foot could be wrapped in a self-contained moist poultice (Animalintex, 3M Animal Care Products Division, St. Paul, Minn.) for 24 hours. Keeping the foot moist renders it more pliable so that movement of the hoof capsule toward a more normal physiologic shape can take place around a central focus, which is the supported coffin bone. The following day when the bandage is removed, the distorted heel will have assumed a more normal position depending on the severity of the condition at the onset. The feet are now trimmed and shod as described previously.

Foals

Sheared heels in foals are usually the result of a rotational deformity of the forelimbs that is often combined with improper trimming. These foals stand toed-out; their outside hoof walls are usually trimmed low regardless of the cause of their problem. If this toed-out stance is a result of outward rotation of the knees, trimming in this manner compounds the problem. Improving the sheared heel involves gradually trimming the foal's hoof level. The correction is done gradually and the affected side is lowered a few millimeters each time the foal is trimmed. If the condition has been severe, the medial heel will have begun to roll under causing a reduction in the ground surface of the hoof. In this case, an extension to the hoof is fabricated with a composite (Equilox International, Pine Island, Minn.) material and is attached to the side of the affected heel, thus increasing the width of the hoof wall. This extension serves two purposes. First, it causes the foal to break over straighter, which improves the limb flight and results in a more uniform strike pattern. Second, the extension prevents further bending of the hoof wall, and adds support to the heel. As the hoof wall grows distally, it will in many cases follow the direction of the composite so that the wall bends less. A large number of these foals will improve as they grow because, as the chest widens, the rotational deformity improves, changing the landing pattern.

PROGNOSIS

The prognosis for this condition is good provided a skilled interested farrier is involved. A committed owner is also necessary because resolution of these cases is slow and ongoing maintenance is often required. Theoretically, the prevention and treatment of lameness caused by inappropriate mediolateral orientation is simple, but in practice it is often difficult to achieve. The knowledge that sheared heels can predispose the horse to multiple hoof wall problems makes prevention imperative. When lameness is localized to a sheared heel or associated with sheared heels, treatment becomes necessary, but sound horses with a sheared heel from whatever cause also will benefit from correction. Many times, improvement is all that can be achieved.



Figure 10.8-4 A horse with a sheared heel shod with a full bar shoe. Note the space between the affected heel and the shoe.

Supplemental Readings

Balch O, White K, Butler D: How lameness is associated with selected aspects of hoof imbalance. Proceedings of the 39th Annual Convention of the American Association of Equine Practitioners, pp 213-214, 1993.

Hickman J, Humphrey M: Hickman's Farriery, 2nd edition, pp 136-182, 195-227, London, JA Allen, 1988.

Moyer W, Anderson JP: Sheared heels: diagnosis and treatment. J Am Vet Med Assoc 1975; 166:53.

Snow V, Birdsall D: Specific parameters used to evaluate hoof balance and support. Proceedings of the 36th Annual Convention of the American Association of Equine Practitioners, pp 299-311, 1990.

Turner TA: The use of hoof measurements for the objective assessment of hoof balance. Proceedings of the 38th Annual Convention of the American Association of Equine Practitioners, pp 389-395, 1992.

Williams G, Deacon M: No Foot, No Horse, pp 1-16, 30-48, 65-80, 99-111, Buckingham, England, Kenilworth Press, 1999.

CHAPTER 10.9

Caudal Heel Pain

BARBARA T. PAGE
Littleton, Colorado

Foot disease accounts for 60% of the lameness in horses. The majority of disease originates from the caudal heel region. The term *caudal heel pain* refers to any pain alleviated with a palmar/plantar digital nerve block and relates to some of the following anatomic structures: the navicular bone (NB), the navicular ligaments, the navicular bursa, the collateral ligaments of the distal interphalangeal joint (DIP), the ungual cartilages, the deep digital flexor tendon (DDFT), the solar and frog corium, the distal laminae, the distal aspect of P3, and the frog. Although more frequently diagnosed in the front limb, caudal heel pain also occurs commonly in the hind limb. Improved diagnostics and radiography have allowed this author to classify caudal heel pain into three etiologic categories: long breakover, contracture of the digital flexor apparatus, and insufficient support of the bony column. Improvements in treatment have improved the outcome and prognosis of caudal heel pain.

LONG BREAKOVER

In this author's opinion, the most common etiology for caudal heel pain is long breakover. Breakover is the most dorsal location of the solar aspect of the hoof capsule that contacts the ground. It is also the last part of the hoof capsule to leave the ground during the caudal phase of the stride.

Breakover can be measured accurately by use of radiography. A long breakover often occurs in a domestic environment because the hoof wall is not eroded away evenly and commensurate with hoof wall growth rate. In the wild, the continually growing hoof wall is eroded as the

horse travels 10 to 20 miles daily. In the domestic environment, erosion of the hoof wall is reduced by metal shoes applied to the hoof wall and because of hand feeding resulting in less travel for grazing. The resultant increase in hoof wall length causes a prying action to occur between the epidermal and dermal laminae, which stimulates the numerous sensory nerves in the laminae.

The research being done by this author, in conjunction with Dr. Robert Bowker and Mr. Gene Ovnicek, theorizes that sensory pain in the laminae causes a reflexive contracture of the flexor apparatus and a steepening of the angle of P1 and P2 to P3, thus misaligning the phalangeal bones and causing a low hoof-pastern axis or broken-back hoof-pastern axis. Vector forces then course less through P3 and more through the NB, the impar ligament, and the wings of P3. Dr. Bowker has documented numerous substance P fibers, the source of pain, in the impar ligament. Pain in the caudal aspect of the heel then results.

Diagnosis

Diagnosis of long breakover includes assessment of stance, movement, hoof capsule shape, and hoof tester evaluation. Radiographic confirmation follows. Horses with a long breakover stand with their front limbs behind the point of their shoulders during the early stages of heel soreness and often point the limb in the later stages. During movement they land flat-footed or toe first and have varying degrees of lameness. Hoof capsules customarily have a lower angle than the pastern angle, with dorsal or palmar/plantar horn tubules forming an angle of less than 50 degrees with the ground. The shape of the sole surface is more oval than square. The distance from the widest measurement on the sole to the toe is longer than the widest measurement of the sole to the heel bulbs. Hoof testers are mildly positive to pressure applied 0.12 cm palmar/plantar to the apex of the frog and over the central third of the frog. Horses land-

The author gratefully acknowledges the assistance of Dr. Gayle Trotter, University of Colorado, in the preparation of this chapter.

Supplemental Readings

Balch O, White K, Butler D: How lameness is associated with selected aspects of hoof imbalance. Proceedings of the 39th Annual Convention of the American Association of Equine Practitioners, pp 213-214, 1993.

Hickman J, Humphrey M: Hickman's Farriery, 2nd edition, pp 136-182, 195-227, London, JA Allen, 1988.

Moyer W, Anderson JP: Sheared heels: diagnosis and treatment. J Am Vet Med Assoc 1975; 166:53.

Snow V, Birdsall D: Specific parameters used to evaluate hoof balance and support. Proceedings of the 36th Annual Convention of the American Association of Equine Practitioners, pp 299-311, 1990.

Turner TA: The use of hoof measurements for the objective assessment of hoof balance. Proceedings of the 38th Annual Convention of the American Association of Equine Practitioners, pp 389-395, 1992.

Williams G, Deacon M: No Foot, No Horse, pp 1-16, 30-48, 65-80, 99-111, Buckingham, England, Kenilworth Press, 1999.

CHAPTER 10.9

Caudal Heel Pain

BARBARA T. PAGE
Littleton, Colorado

Foot disease accounts for 60% of the lameness in horses. The majority of disease originates from the caudal heel region. The term *caudal heel pain* refers to any pain alleviated with a palmar/plantar digital nerve block and relates to some of the following anatomic structures: the navicular bone (NB), the navicular ligaments, the navicular bursa, the collateral ligaments of the distal interphalangeal joint (DIP), the ungual cartilages, the deep digital flexor tendon (DDFT), the solar and frog corium, the distal laminae, the distal aspect of P3, and the frog. Although more frequently diagnosed in the front limb, caudal heel pain also occurs commonly in the hind limb. Improved diagnostics and radiography have allowed this author to classify caudal heel pain into three etiologic categories: long breakover, contracture of the digital flexor apparatus, and insufficient support of the bony column. Improvements in treatment have improved the outcome and prognosis of caudal heel pain.

LONG BREAKOVER

In this author's opinion, the most common etiology for caudal heel pain is long breakover. Breakover is the most dorsal location of the solar aspect of the hoof capsule that contacts the ground. It is also the last part of the hoof capsule to leave the ground during the caudal phase of the stride.

Breakover can be measured accurately by use of radiography. A long breakover often occurs in a domestic environment because the hoof wall is not eroded away evenly and commensurate with hoof wall growth rate. In the wild, the continually growing hoof wall is eroded as the

horse travels 10 to 20 miles daily. In the domestic environment, erosion of the hoof wall is reduced by metal shoes applied to the hoof wall and because of hand feeding resulting in less travel for grazing. The resultant increase in hoof wall length causes a prying action to occur between the epidermal and dermal laminae, which stimulates the numerous sensory nerves in the laminae.

The research being done by this author, in conjunction with Dr. Robert Bowker and Mr. Gene Ovnicek, theorizes that sensory pain in the laminae causes a reflexive contracture of the flexor apparatus and a steepening of the angle of P1 and P2 to P3, thus misaligning the phalangeal bones and causing a low hoof-pastern axis or broken-back hoof-pastern axis. Vector forces then course less through P3 and more through the NB, the impar ligament, and the wings of P3. Dr. Bowker has documented numerous substance P fibers, the source of pain, in the impar ligament. Pain in the caudal aspect of the heel then results.

Diagnosis

Diagnosis of long breakover includes assessment of stance, movement, hoof capsule shape, and hoof tester evaluation. Radiographic confirmation follows. Horses with a long breakover stand with their front limbs behind the point of their shoulders during the early stages of heel soreness and often point the limb in the later stages. During movement they land flat-footed or toe first and have varying degrees of lameness. Hoof capsules customarily have a lower angle than the pastern angle, with dorsal or palmar/plantar horn tubules forming an angle of less than 50 degrees with the ground. The shape of the sole surface is more oval than square. The distance from the widest measurement on the sole to the toe is longer than the widest measurement of the sole to the heel bulbs. Hoof testers are mildly positive to pressure applied 0.12 cm palmar/plantar to the apex of the frog and over the central third of the frog. Horses land-

The author gratefully acknowledges the assistance of Dr. Gayle Trotter, University of Colorado, in the preparation of this chapter.

ing severely toe-first give a positive response to application of hoof testers over the rim of P3.

Confirmation of the diagnosis is through radiography evaluating the bone-to-hoof capsule position and bone characteristics. The method used first requires locating the true apex of the frog. This is the position in which the softer, darker-colored frog meets the harder, lighter-colored sole. A thumbtack is inserted in this location. A radiopaque marker is placed on the dorsal hoof capsule, with the proximal aspect located just where the last hairs leave the skin above the hoof capsule. Both limbs are po-

sitioned on blocks of equal height so that the center of the x-ray beam is over the NB, and the third metacarpal (MCIII) or metatarsal bone (MTIII) is perpendicular to the ground as evaluated using a level placed on mid-MCIII or mid-MTIII. The x-ray beam is directed at right angles to the medial and lateral heel bulbs at a focal/field distance determined for the individual x-ray machine so that image magnification is minimal.

Four measurements are taken from the lateral radiograph to assess bone-to-hoof capsule position (Figure 10.9-1). The bone and hoof capsule are evaluated for

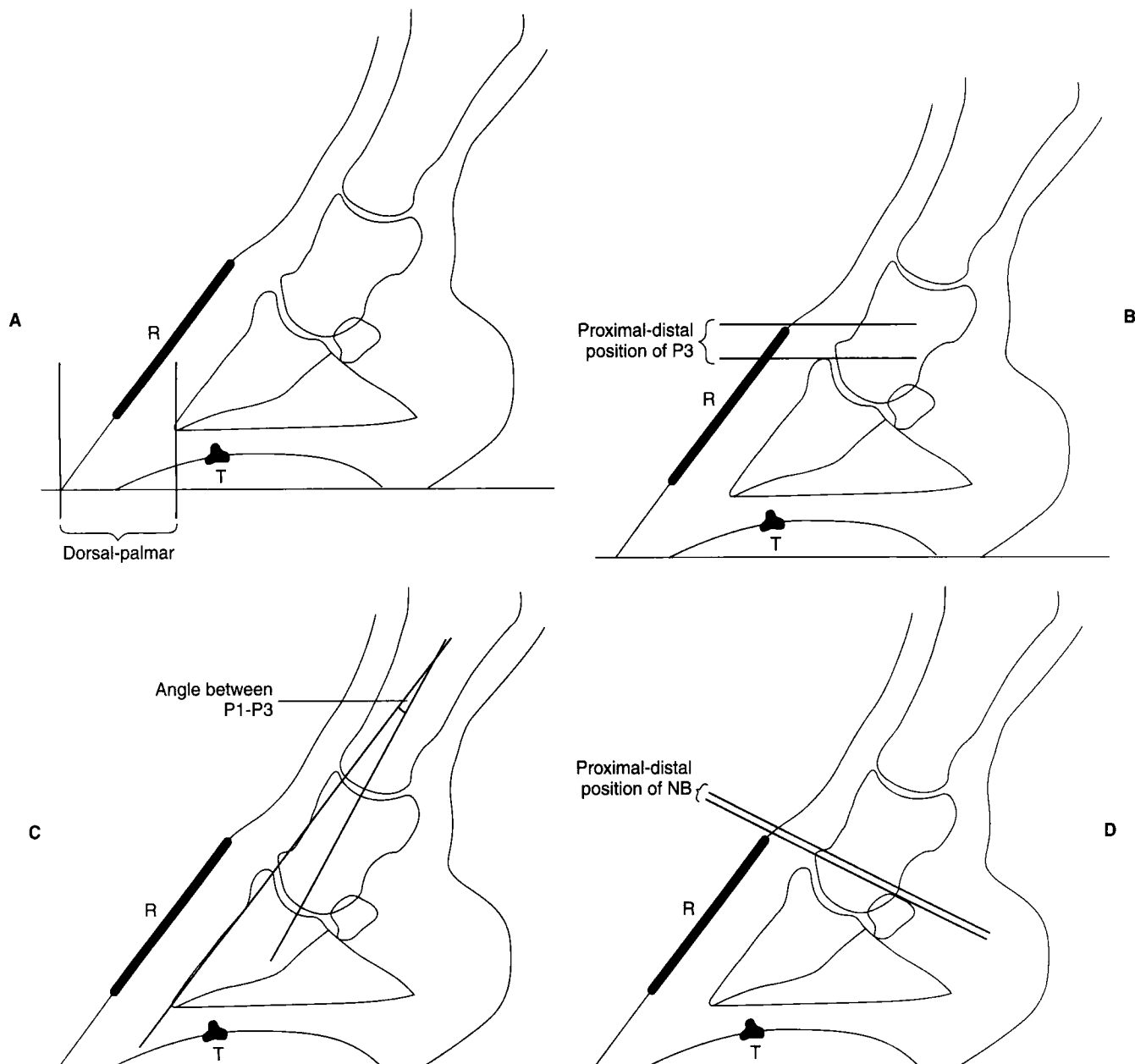


Figure 10.9-1 Diagrams of a lateral radiograph showing how to measure the dorsal-palmar distance (**A**); the proximal-distal position of the third phalanx (P3; **B**); the angle between the first phalanx (P1) and third phalanx (P3; **C**); and the proximal-distal position of the navicular bone (NB; **D**). T, Thumbtack placed where the frog meets the sole; R, radiopaque marker placed on the dorsal hoof capsule with its upper limit where the hairs of the skin meet the hoof wall.

dorsal-palmar position, proximal-distal position of P3, angle between P1 and P3, and the proximal-distal position of the NB. The *dorsal-palmar* distance is determined by measuring from the tip of P3 dorsally to the roll in the hoof capsule or in the shoe, which contacts the wood block. The measured distance between the proximal aspects of the dorsal radiopaque marker to the proximal aspect of the extensor process is the *proximal-distal position of P3*. The angle between a line along the dorsal aspect of P3 and a line bisecting P1 is measured and termed the *P1-P3 angle*. The distance between the joint capsule attachments on P2 and the proximal aspect of the NB is measured and termed the *proximal-distal position* of the NB.

In cases of caudal heel pain secondary to long break-over, the dorsal-palmar distance is greater than 0.6 cm in the front foot and 0.3 cm in the hindfoot in horses weighing between 420 and 550 kg. Concomitant radiographic changes are P1-P3 angle more than 15 degrees and a proximal-distal position of the NB of -2 mm. Bony changes in P3 seen commonly include lipping of the tip of P3, exostosis on the dorsal aspect of P3 that gives a domed appearance to the bone, and osteophytes on the proximal and distal aspect of the NB.

Treatment

The treatment for long breakover in front and hind feet is to position properly the breakover of the shoe or hoof capsule in relationship to P3. The proper position of breakover is 0.6 cm from the tip of P3 in the front foot and 0.3 cm in the hindfoot in horses weighing 420 to 550 kg. Warmbloods require an additional 0.3 cm, and draft horses require an additional 0.6 cm. To determine this position, on the lateral radiograph the distance is measured from the thumbtack to 0.6 cm dorsal to the tip of P3. The same measurement is applied from the tip of the frog dorsally. This marks where the "roll" of the shoe will be placed at application. The dorsal limit of the shoe lies ahead of this mark. Any hoof capsular tissue that extends dorsal to the shoe represents stretched dermal tissue and can be removed safely.

For horses that still do not land heel first after this method of shoeing, isoxsuprine is prescribed at an initial dose of 1.2 mg/kg every 8 hours for 3 weeks. The dose is decreased as soundness improves, to 1.2 mg/kg every 24 hours for 6 weeks, then every other day until heel first landing occurs. Phenylbutazone is added at 200 mg/kg every 12 hours if the lameness is greater than grade II on a scale of I to V, or until recheck at 6 weeks. Injection of therapeutic agents into the distal interphalangeal joint (DIP) or navicular bursa is helpful in longstanding or severe cases.

CONTRACTURE OF THE DIGITAL FLEXOR APPARATUS

Contracture of the flexor apparatus is defined as contracture of the DDFT or the superficial flexor tendon (SFT), or both, and can cause caudal heel pain in congenital or acquired cases. Contracture of the DDFT or "club foot" is most common in the front limbs, but careful examination often reveals a milder form in the diagonal hindlimb.

Contracture can be linked to nutritional imbalances at a young age, congenital abnormalities, or foot pain from various causes, or it can be idiopathic. Pathologic changes that can develop over time include pedal osteitis, strain to the impar ligament, osteophytes of the distal aspect of the NB, and increased vascular channels of the NB. The incidence of contracture can be as high as 25% to 35% in the domestic horse population.

Diagnosis

Horses with contracture frequently are observed standing with the affected front limb placed caudal to the unaffected limb. The stride length is shortened in the affected limb, and lameness is common for the first few strides but then often switches to the opposite limb. Close observation often reveals a number of hoof capsule abnormalities when compared with the opposite limb. These include a steeper hoof capsule, higher heel height, a straighter wall at the quarters, a narrower frog, steeper bars, deeper sulci, and a curl to the palmar aspect of the bars. A broken-forward hoof-pastern axis also may be observed. Application of hoof testers usually reveals greatest sensitivity over the center third of the frog on the affected limb. In longstanding or severe cases in which lameness has shifted to the initially unaffected but overused foot, hoof testers elicit a greater pain response in almost all areas of the foot compared with the initially affected foot.

Radiography can be used to confirm cases having contracture. The previously described method for radiographic technique and evaluation is used. Comparison of bone-to-hoof capsule position between the contracted and noncontracted limb reveals the following on the contracted limb: subluxation between P2 and P3 or between P1 and P2, a greater angle between the ground and the solar aspect of P3, a more proximal position of the NB relative to the joint capsule attachment of distal P2, a smaller angle between the dorsal aspect of P3 and a line bisecting P1, and a greater angle from the dorsal aspect of P3 to the ground. Bony radiographic changes may include pedal osteitis, spurring of the distal aspect of the NB, an increase in vascular channels of the NB, occasionally rim fractures of P3 and often an exostosis at the midsection of the solar aspect of P3.

Treatment

Treatment for contracture includes shoeing, medication, or surgery. Therapeutic shoeing ensures breakover is positioned 0.6 cm from the tip of P3 and elevates the heel by using a wedge shoe, wedge pad, or the Equine Digit Support System (EDDS, Inc., Penrose, Colo.) to a height at which the foot lands heel-first. Isoxsuprine (1.2 mg/kg q24h) is used concurrently. If after 6 to 12 weeks heel-first landing has not been achieved, an accessory carpal ligament resection may be considered. This procedure results in a decreased angle of P3 to the ground and movement of the NB more distally within a few hours after surgery. Long-term results are improved by lowering the heel to the widest part of the frog every 2 weeks for 6 weeks. Over the next 4 to 6 months, weight bearing and stance become more equal. Wedging of the contracted limb may

still be necessary temporarily or permanently, but to a lesser degree. This surgical procedure improves both the lameness and the way of going in horses of any age, although greater improvement is noted in younger horses.

INSUFFICIENT SUPPORT OF THE BONY COLUMN

The third common cause of caudal heel pain is insufficient support under the bony column. This lack of support is present to some degree in any horse in which the frog is not in contact with the ground, but it is most prominent in horses with thin-walled hooves and small feet. This problem may also occur in the hind feet of dressage horses. In natural environments the bony column is supported through frog contact with the ground and through dirt compacted into the sulci. Application of a shoe, which is necessary in most domestic environments, transfers the mass of the horse away from the center of the limb to the periphery of the foot that is the hoof wall, a tissue of epidermal origin not designed to support mass. Without support through the center of the hoof, collapse of the caudal heel occurs, creating a broken-back hoof-pastern axis with an associated increase in strain to the DDFT at its insertion onto P3—and, theoretically, compression of the vasculature with the impar ligament. Concurrent changes are a distal descent of P3 within the hoof capsule, with an associated increase in strain to the laminae in a proximal/distal direction, along with a more distal location of the NB, with an associated increase in strain to the navicular ligaments.

Diagnosis

Horses with insufficient support usually stand with the front limb behind the point of the shoulder so that their weight is borne over the more dorsal aspects of the hoof. Stride length shortens, and lameness varies from grades I to IV/V, being most marked when the horse is circled tightly. Hoof capsule characteristics include the following:

- A hoof capsule angle at the heel of less than 45 degrees (often between 15-30 degrees)
- Heel pillars that are dorsal to the base of the frog
- Hoof walls that curl axially at the heel bulbs
- A thin hoof wall
- A narrow frog with deep sulci

In the hind feet the frog may be enlarged because it has adapted to meet the body's need for increased support. Application of hoof testers elicits a positive response over the bars and the center third of the frog and over the rim of P3 if the horse is landing excessively toe-first.

Radiographs should be evaluated for bone-to-hoof capsule position and bone characteristics. Findings are generally similar to those seen in long breakover, but the breakover distance is normal. Using the previously described method, common findings include the following:

- The proximal-distal position of P3 greater than 1.2 cm
- A measured angle between P1 and P3 of greater than 15 degrees

- The proximal-distal position of the NB less than –2 mm
- The proportion of length of the solar aspect of P3 to the distance from the wing of P3 to the heel bulb less than two parts bone to one part heel bulb
- A shallow sole depth

Changes in bone shape include exostosis of the wings of P3, creating a concave shape to the solar aspect of P3, osteophytes of the proximal and distal aspects of the NB, and increased synovial invaginations of the NB.

Treatment

Treatment is the same for the front and hind feet and consists of application of breakover as described previously and support for the center of the mass, which lies beneath the frog. If the environment is uniform and not overly rocky or pebbly, mild cases may respond to removing the shoe, not removing any sole tissue, and rasping any hoof wall that grows beyond the level of the sole every 3 weeks, and not removing dirt that packs into the sulci. Treatment is continued for 3 to 6 months or until the sole cups and thickens and the frog enlarges. Therapeutic shoeing is used in more severe cases. The center of mass is supported through the frog artificially first by use of dental impression material in the sulci and over the frog and then application of a firm wedge pad and shoe. If the horse still does not land heel first, a higher wedge can be used using either a steeper wedge pad or the EDSS system. When the horse does land heel first, a rectangular or triangular frog insert is attached to the wedge pad in the location of the base of the frog. This pad is thick enough so that the frog insert contacts the ground when the horse is standing.

This shoeing method is used for the length of the career of the horse or until the foot becomes healthy, as indicated by a cupping of the sole, a thickening of the sole depth, and an increased size of the frog accompanied by a decrease in lameness. Concurrent use of isoxsuprine as previously described is used adjunctively. Therapeutic medications placed into the DIP joint are helpful in long-standing cases.

Supplemental Readings

Ovnicek GD, Erfle JB, Peters DF: Wild horse hoof patterns offer a formula for preventing and treating lameness. *Proceedings of the 41st Annual Convention of the American Association of Equine Practitioners*, pp 258-260, 1995.

Page BT: Breakover of the hoof and its influence on the structure and forces within the foot. *J Equine Vet Sci* 2002; 22:258-264.

Wilson AM: The biomechanical effect of wedged, eggbar, and extension shoes in sound and lame horses. *Proceedings of the 47th Annual Convention of the American Association of Equine Practitioners*, pp 339-343, 2001.

Wright IM, Douglas J: Biomechanical considerations in the treatment of navicular disease. *Vet Rec* 1993; 133:109-114.

CHAPTER 10.10

Upward Fixation of the Patella

SHANE M. MILLER
TERRY D. SWANSON
Littleton, Colorado

Upward fixation of the patella (UFP) is a condition commonly seen in young horses and ponies. This condition can also be seen in older horses that are changing careers if they are not fit for that new discipline. UFP occurs when the medial patellar ligament fails to disengage from the medial trochlear ridge of the femur.

In the severe form of UFP, the limb becomes fixed in extension with the horse dragging the limb. More commonly, in mild cases there is a partial or intermittent "catching" of the patella that results from a delayed release of the patella. The failure in disengagement of the patella is caused by a failure of the quadriceps muscle group to pull the patella up and off the medial trochlear ridge of the femur. UFP is thought to occur most often in horses with straight hind limb conformation, which suggests a possible heritable component. Horses in poor muscular condition are also affected. Fixation can be exaggerated when horses travel downhill, movement that elicits a hyperextension of the limb. The typical presentation is a young horse beginning training, an older horse changing careers in poor muscle fitness, or a horse convalescing from musculoskeletal conditions can show signs when they return to exercise. Stall confinement is discouraged because of potential loss of muscle tone.

CLINICAL SIGNS

The clinical signs of UFP are variable depending on the severity of the case. In mild cases of delayed patellar release, a "catching" of the stifle occurs, followed by a hyperflexion response. This response will present as a noted lameness that improves within a couple of strides. It is seen most often in short, tight circles or when the horse decelerates between gaits. Horses may stumble or knuckle over on one or both rear legs and may be reluctant to go straight downhill; excessive wear of the dorsal hoof wall may also be seen. In the severe form of UFP the limb is in full extension and unable to release the patella. The horse usually carries the limb behind, the patellar ligaments are tense, and wearing of the toe can be evident.

DIAGNOSIS

A detailed history is very valuable in establishing a diagnosis of subtle UFP, because the horse may not exhibit lameness between episodes. If the horse is evaluated at a walk, in slow tight circles, backing up, downhill, and decelerating between gaits, UFP can be exacerbated. During partial fixation, an audible clicking sound may be heard.

The horse may travel with lameness in the affected limb for a few strides before soundness returns. Western horses moving at a slow jog may show an excessively shortened anterior stride with an otherwise sound gait. At the trot, the gait can be more mechanical and without painful lameness, except in chronic cases. These horses often are not expected to improve with nonsteroidal antiinflammatory drugs. Subtle cases can also be a compensation for another type of lameness. If the clinician holds the patella over the medial trochlear ridge and walks the horse forward, the patella may lock. If the patella can be held in this position momentarily, a diagnosis of UFP can be suspected.

TREATMENT

In intermittent cases, the hallmark of therapy is to develop the quadriceps muscle group to pull the patella proximally and release the patella from the medial trochlear ridge. Altering the conditioning program can be helpful to gain adequate quadriceps function. The conditioning should include long, extended, straight exercises. Uphill work with limited downhill work in good footing is encouraged, but deep soil should be avoided no matter the type of exercise. Work that involves slow tight circles should also be avoided. With caution, heel-elevated shoes or shoes with wedge pads can also be used to help with intermittent fixation but may worsen horses with low pastern angles. Egg bar type shoes often result in moderate heel elevation as well.

Counterirritant injections along the medial and middle patellar ligaments are used in cases of intermittent UFP. The injections are performed with the horse standing and sedated, and the counterirritant is injected within the medial and lateral borders of each ligament just proximal to the tibial insertion. A total of 2 ml at each site is used. The needle is inserted close to the tibial insertion in a dorsal direction along and within the ligament border and the counterirritant is injected while the needle is withdrawn. Common counterirritants would include 2% iodine (in various forms of adjuvants), or volatile salts such as Triple Block (Triple Crown, Lexington, Ky.) or ser-apin. The exact mechanism of action remains unknown; however, the irritant is thought to cause inflammation and thus tighten the ligament, hindering fixation on the femur. Swelling after injection can be expected for a few days. It is very important that exercise continue after injection to build muscle tone, and that nonsteroidal anti-inflammatory agents be given during this period to help

improve the comfort level. The therapy is often repeated two to three times as needed.

A treatment that is currently preferred is systemic estrogen therapy. Although the mechanism of action is unknown, it is postulated that the systemic estrogens relax the peripelvic muscles and ligaments thus altering the angle of the pelvis. The alteration in pelvic angle may decrease the stifle joint angle and thus enable the patella to release from the femur. The systemic estrogen regime is as follows: estrogen is administered intramuscularly starting at 20 mg weekly for 3 to 4 weeks. The dose is then decreased in 5 mg increments weekly down to 10 to 15 mg. If intermittent fixation returns at the lower dose, then the dose should be increased. The length of treatment is 6 to 8 weeks but can be extended, and it is crucial that exercise continue through the therapy to build muscle tone. This therapy has been very effective for these authors and minimizes the use of counterirritants.

Transection of the medial patellar ligament is therapy that has historically been recommended but should be reserved for cases unresponsive to all other treatments and used as a last resort. Desmotomy of the medial patellar ligament is performed in the standing, sedated patient. The stifle area is clipped and surgically prepped. The tail should be wrapped and tied to the neck to avoid contact with the surgical area. A local anesthetic is injected subcutaneously between the middle and medial patellar ligaments and into the medial patellar ligament. A 1-cm skin

incision is made between the middle and medial patellar ligaments, the medial patellar ligament is isolated and transected with a curved bistoury. The skin is then apposed with skin sutures. The horse is confined to a stall postoperatively with walking exercise beginning 2 weeks after surgery. Light exercise should begin 6 to 8 weeks after surgery. This procedure has fallen out of favor because of the complications that have arisen (e.g., osteoarthritis, distal patellar fragmentation, and chondromalacia of the patella).

A new treatment has been recently described in a small number of horses. The surgery involves an ultrasound-guided approach for percutaneous splitting of the proximal one third of the medial patellar ligament. This procedure is thought to induce a desmitis that prohibits the patella from locking on the medial trochlear ridge, reducing the potential for upward fixation.

Supplemental Readings

Sullins, SE: The Stifle. In Stashak TS (ed): *Adams' Lameness in Horses*, 5th edition, pp 1022-1025, Philadelphia, Lippincott Williams & Wilkins, 2002.

Tnibar AM: Medial patellar ligament splitting for the treatment of upward fixation of the patella. *Proceedings of the 47th Annual Convention of the American Association of Equine Practitioners*, pp 491-493, 2001.

CHAPTER 10.11

Osseous Sequestra

EARL M. GAUGHAN
Manhattan, Kansas

The sequestration of cortical bone delays wound healing and, depending on location, can place other tissues at risk. Osseous sequestra are defined as cortical bone that has lost local vascular perfusion. This loss leads to subsequent formation of the classic structures that define a sequestrum. These structures include the sequestrum itself (devitalized cortical bone), the involucrum (the productive, remodeled bone that immediately surrounds the devitalized bone fragment), and the cloaca (outflow tract in bone), a draining tract in soft tissue and purulent exudate (Figure 10.11-1).

A sterile sequestrum in the absence of a soft tissue wound is theoretically possible; however, sequestra in horses should be considered contaminated and infected. Days to weeks, or more, of wound healing delay can be anticipated after degloving injury when cortical bone is devitalized and sequestration occurs.

Identification and diagnosis of sequestra are reasonably straightforward. The likelihood that a sequestrum will

form should be considered high with any degloving injury that exposes cortical bone and any other substantial trauma that penetrates to cortical bone. The main frustration in sequestra management is the delay in identification of the problem and the resulting delay in wound healing. It usually takes 10 to 14 days for sequestra to become radiographically apparent. This period also coincides with the time to clinical definition and appearance of the sequestered fragment of cortical bone. Therefore ideal treatment should be initiated in a manner to make appropriate wound healing as brief as possible.

Some untreated cortical sequestra will ultimately be extruded by the formation of granulation tissue and purulent exudate. However, overlying soft tissues and the formation of a substantial involucrum can restrict this process and result in a chronic draining tract. This typical clinical scenario usually requires surgical treatment to remove sequestered bone. The ultimate goal for treatment of cortical sequestra is removal of the devitalized bone.

improve the comfort level. The therapy is often repeated two to three times as needed.

A treatment that is currently preferred is systemic estrogen therapy. Although the mechanism of action is unknown, it is postulated that the systemic estrogens relax the peripelvic muscles and ligaments thus altering the angle of the pelvis. The alteration in pelvic angle may decrease the stifle joint angle and thus enable the patella to release from the femur. The systemic estrogen regime is as follows: estrogen is administered intramuscularly starting at 20 mg weekly for 3 to 4 weeks. The dose is then decreased in 5 mg increments weekly down to 10 to 15 mg. If intermittent fixation returns at the lower dose, then the dose should be increased. The length of treatment is 6 to 8 weeks but can be extended, and it is crucial that exercise continue through the therapy to build muscle tone. This therapy has been very effective for these authors and minimizes the use of counterirritants.

Transection of the medial patellar ligament is therapy that has historically been recommended but should be reserved for cases unresponsive to all other treatments and used as a last resort. Desmotomy of the medial patellar ligament is performed in the standing, sedated patient. The stifle area is clipped and surgically prepped. The tail should be wrapped and tied to the neck to avoid contact with the surgical area. A local anesthetic is injected subcutaneously between the middle and medial patellar ligaments and into the medial patellar ligament. A 1-cm skin

incision is made between the middle and medial patellar ligaments, the medial patellar ligament is isolated and transected with a curved bistoury. The skin is then apposed with skin sutures. The horse is confined to a stall postoperatively with walking exercise beginning 2 weeks after surgery. Light exercise should begin 6 to 8 weeks after surgery. This procedure has fallen out of favor because of the complications that have arisen (e.g., osteoarthritis, distal patellar fragmentation, and chondromalacia of the patella).

A new treatment has been recently described in a small number of horses. The surgery involves an ultrasound-guided approach for percutaneous splitting of the proximal one third of the medial patellar ligament. This procedure is thought to induce a desmitis that prohibits the patella from locking on the medial trochlear ridge, reducing the potential for upward fixation.

Supplemental Readings

Sullins, SE: The Stifle. In Stashak TS (ed): *Adams' Lameness in Horses*, 5th edition, pp 1022-1025, Philadelphia, Lippincott Williams & Wilkins, 2002.

Tnibar AM: Medial patellar ligament splitting for the treatment of upward fixation of the patella. *Proceedings of the 47th Annual Convention of the American Association of Equine Practitioners*, pp 491-493, 2001.

CHAPTER 10.11

Osseous Sequestra

EARL M. GAUGHAN
Manhattan, Kansas

The sequestration of cortical bone delays wound healing and, depending on location, can place other tissues at risk. Osseous sequestra are defined as cortical bone that has lost local vascular perfusion. This loss leads to subsequent formation of the classic structures that define a sequestrum. These structures include the sequestrum itself (devitalized cortical bone), the involucrum (the productive, remodeled bone that immediately surrounds the devitalized bone fragment), and the cloaca (outflow tract in bone), a draining tract in soft tissue and purulent exudate (Figure 10.11-1).

A sterile sequestrum in the absence of a soft tissue wound is theoretically possible; however, sequestra in horses should be considered contaminated and infected. Days to weeks, or more, of wound healing delay can be anticipated after degloving injury when cortical bone is devitalized and sequestration occurs.

Identification and diagnosis of sequestra are reasonably straightforward. The likelihood that a sequestrum will

form should be considered high with any degloving injury that exposes cortical bone and any other substantial trauma that penetrates to cortical bone. The main frustration in sequestra management is the delay in identification of the problem and the resulting delay in wound healing. It usually takes 10 to 14 days for sequestra to become radiographically apparent. This period also coincides with the time to clinical definition and appearance of the sequestered fragment of cortical bone. Therefore ideal treatment should be initiated in a manner to make appropriate wound healing as brief as possible.

Some untreated cortical sequestra will ultimately be extruded by the formation of granulation tissue and purulent exudate. However, overlying soft tissues and the formation of a substantial involucrum can restrict this process and result in a chronic draining tract. This typical clinical scenario usually requires surgical treatment to remove sequestered bone. The ultimate goal for treatment of cortical sequestra is removal of the devitalized bone.

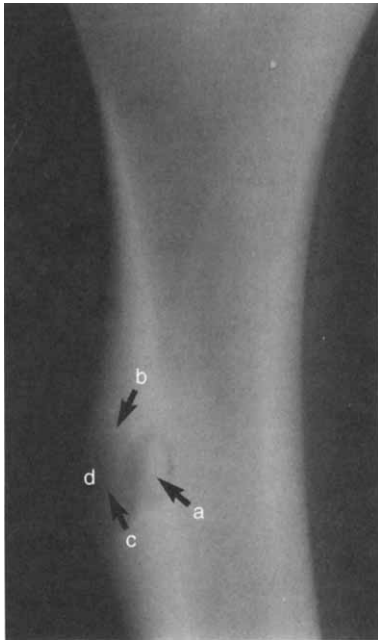


Figure 10.11-1 A lateral radiographic projection of the metacarpal region of a horse demonstrating the radiographic appearance of the classic structures associated with an osseous sequestrum. *a*, Sequestrum; *b*, involucrum; *c*, cloaca; *d*, draining tract.

Normal granulation tissue and epithelial cells will not migrate over devascularized tissues and, therefore, such a wound will not appropriately heal. Once the devitalized bone is removed from its sequestered location, wound healing can progress to completion.

The exposed nature of the distal limbs of horses renders these regions prone to the type of trauma that result in sequestration of cortical bone. The dorsal aspects of the third metatarsal and metacarpal bones are very common sites for this process to occur. However, cortical bone in any location can be affected if the trauma is adequate to compromise exterior cortical blood flow. Care should be exercised in the assessment of sequestra because it is imperative to understand which tissues have been wounded and which tissues may be disrupted in attempts to remove a sequestrum. Caution is especially important with bone—that is, supporting soft tissue attachments (e.g., joint capsule and ligament).

It is commonly stated that the interior two thirds of the blood flow to cortical bone derives from endosteal vessels and the superficial one third from periosteal vessels. It has also been suggested, however, that most of the blood flow to adult cortical bone is from endosteal origins. The latter appears to be more likely given that the typical sequestrum occupies less than one third of cortical thickness. Crushing trauma also appears necessary as a component of the wounding episode; simple exposure of cortical bone by elevation of periosteum does not result in sequestration. Recognition of this fact may be influential in the selection of treatment and potentially in preventive measures against sequestrum formation.

Superficial cortical bone may behave in several manners after wounding. Wounds may heal without a clini-

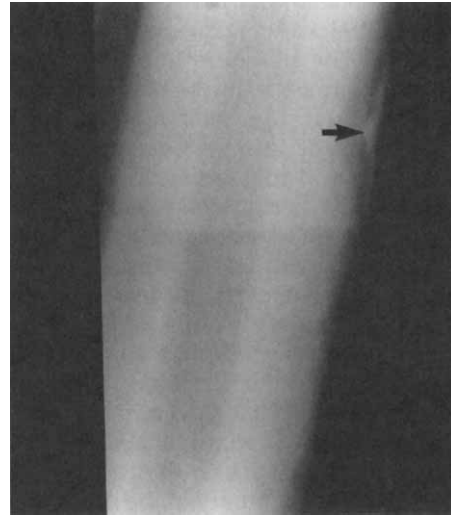


Figure 10.11-2 A lateral radiographic projection of the metacarpal region of a horse. A type 1 sequestrum of superficial cortical bone is present.

cally important response from bone, although this is not common in horses. Injured bone may form a typical osseous sequestrum of hard, devitalized cortical bone. Less common is mineralization of the superficial aspects of a wounded bone surface. This tissue grossly appears like woven bone or mineralized granulation tissue. It may indeed be both. This author's experience indicates this is most common after wounding of the distal limbs. This type of osseous response clinically resembles the more typical sequestrum with delayed wound healing and associated exudate. The characteristics of the two responses to injury have prompted the suggestion that two types of sequestra may exist. Type 1 is characterized by a separated, devitalized fragment of cortical bone (Figure 10.11-2), and type 2 is characterized by broadly attached, soft, or woven mineralized tissue that overlies the parent bone at the wound site (Figure 10.11-3).

TREATMENT

Medical treatment of osseous sequestra is rarely successful as the sole form of therapy. Local and systemic antibiotic therapy may reduce complications, address wound site seeding of contaminants to distant locations, and reduce the volume of exudate. Systemic treatment is encouraged after acute wounding until the establishment of granulation tissue throughout the wound site. The presence of granulation tissue can often guide the discontinuation of systemic antibiotic therapy. However, antibiotic therapy can markedly influence the clinical signs associated with the presence of chronic sequestra. The purulent exudate from a draining tract associated with a sequestrum can be reduced and eliminated with antibiotics. Yet when antibi-

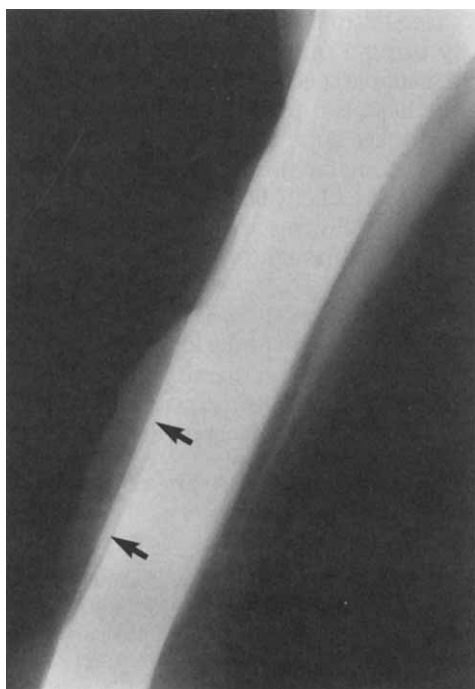


Figure 10.11-3 A lateral radiographic projection of the metacarpal region of a horse. A type 2 sequestrum is present. Note the superficial, broadly attached, loosely mineralized tissue over the denuded parent bone.

otics are discontinued, the purulent exudate recurs because the sequestrum stimulating the tract has not been addressed.

Antibiotic therapy alone rarely successfully resolves local sepsis associated with cortical bone in horses. An early, accurate diagnosis or recognition of the high likelihood of cortical sequestration is necessary for cost-effective treatment.

The definitive treatment of a sequestrum is its removal. This removal generally allows complete unimpeded second intention wound healing or successful delayed primary closure. Depending on the location of the sequestrum and timing to presentation, surgical removal can be accomplished with a horse either standing or recumbent under general anesthesia. Often granulation tissue overlies sequestered bone and therefore may impede observation of the surgical site. For this reason this author removes most sequestra from horses under general anesthesia.

Placement of a tourniquet proximal to the surgical site can reduce intraoperative hemorrhage. Surgical removal of a sequestrum can be as simple as the operator identifying the affected horse, grasping the sequestrum, and elevating it from the wound site. However, most sequestra require more aggressive manipulation. When a substantial involucrum is present, debridement of the reactive bone usually is required to expose the sequestrum and elevate the devitalized bone. This task can be completed with a hand curette or motorized burr. Total resection of the involucrum usually is not necessary and may not be desirable. Exposure that is substantial enough for the removal of the sequestrum is the goal.

Due to expected remodeling of cortical bone after sequestrectomy and return to exercise, excessive removal of



Figure 10.11-4 Partial-thickness drilling of 2.7-mm holes is an attempt to prevent sequestration of superficial cortical bone.

vascularized cortical bone is not encouraged. Wound closure is optional. Occasionally, sequestra can be resected and associated soft tissue closed. Second-intention healing and wound management are usually the most satisfactory steps, as the region is contaminated and drainage is desired. Placement of a passive or active drain is not often indicated and can complicate otherwise straightforward granulation, contraction, and epithelialization. Bandaging of distal limb wounds is encouraged until second-intention healing is considered completed.

PREVENTION

Prevention of the sequestration of cortical bone after wounding would be very beneficial in reducing time to healing and cost to clients. Although controlled experiments on sequestrum prevention have not been conducted, prospective treatment attempts suggest that prevention may be possible in some cases. Timely manipulation is necessary, with the goal to provide successful vascular perfusion into the bone that has lost its blood supply. This goal requires the clinician to access local and regional vascular supply and establish a route for neovascularization of the potentially sequestered bone.

This author has used two methods to attempt to avoid sequestrum formation. The osteostixis that has been successful in assisting dorsal cortical fracture healing in the third metacarpal bone has been modified to prevent sequestrum formation. Drilled "wells" of 2.7 mm or $\frac{1}{8}$ inch have replaced the full-thickness cortical drillings (Figure 10.11-4). This procedure accesses the endosteal blood supply to deeper cortical bone. If successful, the procedure can allow neovascularization of the denuded, superficial cortical bone. If this is done before necrosis occurs, salvage of cortical bone and prevention of sequestration may be possible. A pneumatic surgical drill or a sterilized electrical hand drill is used with 2.7 mm or $\frac{1}{8}$ -inch drill bits. Holes are drilled to form a mosaic pattern with holes no closer than 0.5 cm apart. This procedure can be performed in standing, sedated horses or with the horse under general anesthesia. This author has the impression that a number of cases did not sequester bone when it would have otherwise been fully expected. Partial-thickness drillings have

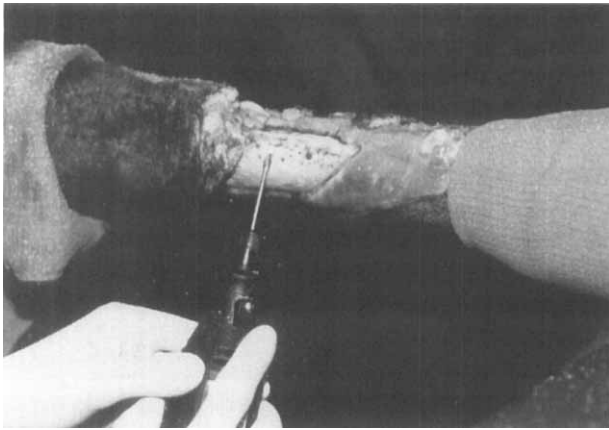


Figure 10.11-5 A high-speed burr is being used to remove superficial traumatized bone. Note the hemorrhage present on the bone surface after curettage.

been used to avoid contamination of the medullary cavity; however, this may not be essential.

The second method used to avoid sequestration is intended to rid the wound site of a potential sequestrum and allow wound healing to progress unimpeded. Because the geometry of a sequestrum is defined by the edges of the normal periosteum, a high-speed burr has been used to debride the exposed cortical bone to a level producing ready osseous hemorrhage. In essence, this method performs the sequestrectomy before the sequestrum forms (Figure 10.11-5). The debridement is shallow and not

likely to exceed 2 to 3 mm. Debridement can be accomplished by using a pneumatic surgical bone burr, or a hand-held, variable speed, burring tool with a surgical bit. This author has been pleased that this method has allowed appropriate bone and wound healing to progress when most parameters indicated sequestration and delayed healing were likely. Both of these methods are suggested from clinical cases and have not been proven by original research, although prospective case review is under way.

The prognosis for most osseous sequestra in horses is good to excellent. The anatomic location certainly dictates the prognosis because sequestered bone that undermines joint capsule and ligamentous associations can greatly complicate treatment and prognosis.

Supplemental Readings

- Clem MF, DeBowes RM, Yovich JV et al: Osseous sequestration in the horse: a review of 68 cases. *Vet Surg* 1988; 17:2-5.
- Clem MF, DeBowes RM, Yovich JV et al: Osseous sequestration in horses. *Comp Cont Educ Pract Vet* 1987; 9:1219-1225.
- Jann HW, Peyton LC, Fackelman GE: The pathogenesis and treatment for traumatically induced sequestra in horses. *Comp Cont Educ Pract Vet* 1987; 9:181-188.
- Lee AH, Swaim SF, Newton JC et al: Wound healing over denuded bone. *J Am Anim Hosp Assoc* 1987; 23:75-84.
- Specht TE, Miller GJ, Colahan PT: Effects of clustered drill holes on the breaking strength of the equine third metacarpal bone. *Am J Vet Res* 1990; 51:1242-1246.

CHAPTER 10.12

Surgical Options to Alleviate Pain of the Distal Tarsal Joints

BRENT A. HAGUE
Edmond, Oklahoma

Degenerative joint disease of the distal tarsal joints is a significant source of lameness in all disciplines of horses. Clinical signs of distal tarsal arthritis are variable and may include gait abnormalities typical for tarsal lameness, including accentuated elevation of the affected limb, shortened cranial phase of the stride, and decreased arc of the foot, and the lameness is usually exacerbated after a hindlimb flexion test. The lumbar and gluteal region of these horses also can become painful secondary to the abnormal gait. Radiographic changes may not be correlated directly with severity of lameness; consequently, the diagnosis of distal tarsal pain should be verified with intraarticular anesthesia of both the distal intertarsal and

tarsometatarsal joints. Without proper treatment, performance diminishes and objectionable habits, such as refusing to turn a barrel pattern, often develop.

Many treatment options have been developed to alleviate tarsal pain, most of which are focused on decreasing the inflammation in the affected joints. Nonsteroidal antiinflammatory medications and the use of intraarticular medications, such as corticosteroids and hyaluronic acid, are common. Horses that become refractory to this form of treatment often require surgical treatment to achieve soundness. The intent of this chapter is to discuss various surgical treatment options that alleviate pain of the distal tarsal joints.



Figure 10.11-5 A high-speed burr is being used to remove superficial traumatized bone. Note the hemorrhage present on the bone surface after curettage.

been used to avoid contamination of the medullary cavity; however, this may not be essential.

The second method used to avoid sequestration is intended to rid the wound site of a potential sequestrum and allow wound healing to progress unimpeded. Because the geometry of a sequestrum is defined by the edges of the normal periosteum, a high-speed burr has been used to debride the exposed cortical bone to a level producing ready osseous hemorrhage. In essence, this method performs the sequestrectomy before the sequestrum forms (Figure 10.11-5). The debridement is shallow and not

likely to exceed 2 to 3 mm. Debridement can be accomplished by using a pneumatic surgical bone burr, or a hand-held, variable speed, burring tool with a surgical bit. This author has been pleased that this method has allowed appropriate bone and wound healing to progress when most parameters indicated sequestration and delayed healing were likely. Both of these methods are suggested from clinical cases and have not been proven by original research, although prospective case review is under way.

The prognosis for most osseous sequestra in horses is good to excellent. The anatomic location certainly dictates the prognosis because sequestered bone that undermines joint capsule and ligamentous associations can greatly complicate treatment and prognosis.

Supplemental Readings

- Clem MF, DeBowes RM, Yovich JV et al: Osseous sequestration in the horse: a review of 68 cases. *Vet Surg* 1988; 17:2-5.
 Clem MF, DeBowes RM, Yovich JV et al: Osseous sequestration in horses. *Comp Cont Educ Pract Vet* 1987; 9:1219-1225.
 Jann HW, Peyton LC, Fackelman GE: The pathogenesis and treatment for traumatically induced sequestra in horses. *Comp Cont Educ Pract Vet* 1987; 9:181-188.
 Lee AH, Swaim SF, Newton JC et al: Wound healing over denuded bone. *J Am Anim Hosp Assoc* 1987; 23:75-84.
 Specht TE, Miller GJ, Colahan PT: Effects of clustered drill holes on the breaking strength of the equine third metacarpal bone. *Am J Vet Res* 1990; 51:1242-1246.

CHAPTER 10.12

Surgical Options to Alleviate Pain of the Distal Tarsal Joints

BRENT A. HAGUE
 Edmond, Oklahoma

Degenerative joint disease of the distal tarsal joints is a significant source of lameness in all disciplines of horses. Clinical signs of distal tarsal arthritis are variable and may include gait abnormalities typical for tarsal lameness, including accentuated elevation of the affected limb, shortened cranial phase of the stride, and decreased arc of the foot, and the lameness is usually exacerbated after a hindlimb flexion test. The lumbar and gluteal region of these horses also can become painful secondary to the abnormal gait. Radiographic changes may not be correlated directly with severity of lameness; consequently, the diagnosis of distal tarsal pain should be verified with intraarticular anesthesia of both the distal intertarsal and

tarsometatarsal joints. Without proper treatment, performance diminishes and objectionable habits, such as refusing to turn a barrel pattern, often develop.

Many treatment options have been developed to alleviate tarsal pain, most of which are focused on decreasing the inflammation in the affected joints. Nonsteroidal antiinflammatory medications and the use of intraarticular medications, such as corticosteroids and hyaluronic acid, are common. Horses that become refractory to this form of treatment often require surgical treatment to achieve soundness. The intent of this chapter is to discuss various surgical treatment options that alleviate pain of the distal tarsal joints.

CUNEAN TENECTOMY

The cunean tendon is a medial extension of the cranial tibialis muscle that inserts distally on the first and second tarsal bones. Tension on the cunean tendon during weight bearing is thought to exert torsional forces on the lower tarsal joints; therefore removal of a section of the cunean tendon may decrease rotation of the lower joints and thus decrease pain.

The procedure is performed on the standing sedated horse under local anesthetic injected in an inverted V pattern just proximal to the palpable cunean tendon on the medial aspect of the tarsus. A 2-cm vertical skin incision is made over the tendon, and a curved hemostat is used to isolate and elevate the tendon from the incision. A 1-cm section of tendon is removed, and the skin apposed with simple interrupted sutures using a nonabsorbable suture material. A light bandage, consisting of a sterile telfa pad and elasticon are placed over the surgery site with a cotton support wrap applied over the light bandage for the first 48 hours after surgery to decrease swelling.

Postoperatively, the horse is confined to a stall for 12 days, with daily hand-walking for 20 minutes. After 12 days, the interval of hand-walking is increased to 30 minutes a day for an additional 10 days. Horses should be made to walk over poles on the ground or provided with some form of exercise that requires the horse to flex the tarsus. Riding begins approximately 3 weeks after surgery and should include work over obstacles to make the horse maximally flex the tarsus. Regular work can be resumed 6 weeks after surgery. The surgery site may be slightly enlarged for approximately 2 to 3 months. Approximately 6 months after the procedure, most horses have little if any cosmetic blemish.

The success rate of cunean tenectomy varies depending on the surgeon evaluating the procedure. An owner survey of 285 cases of bone spavin treated by cunean tenectomy showed 83% of owners believed that lameness and performance improved after the surgery and that they would have the procedure performed again. The success of this procedure is related directly to strict adherence to exercise protocols in the convalescent period. Exercise of horses over obstacles and early return to consistent exercise seem to be the most important factors.

FENESTRATION

The pathogenesis of distal tarsal pain is likely multifactorial, including joint capsule synovitis, subchondral pain, and pain caused from increased intraosseous pressure. Some horses with characteristic gait abnormalities attributable to distal tarsal pain exhibit minimal to no radiographic change yet become sound with intraarticular anesthesia of the distal intertarsal and tarsometatarsal joint. If the pain were eliminated easily long term (4 to 6 months) with intraarticular therapy using hyaluronic acid and a low dose of corticosteroid, then a diagnosis of primary synovitis would be most likely. However, a large percentage of the horses seen by the author are referred with a history of minimal response to repetitive intraarticular therapy and no radiographic evidence of degenerative joint disease of the distal tarsal joints. Intraosseous pressures greater than 45 mm Hg in the tarsal cuboidal bones

are associated with pain. Therefore tarsal fenestration in these cases should provide decompression of the cuboidal bones and alleviate pain.

The surgical technique used by the author differs from the currently described technique. The horse is positioned in dorsal recumbency under general anesthesia with the hind limbs suspended from stands, which allows easy access to the medial aspect of the tarsus. The limb is clipped circumferentially from mid-tibia to mid-cannon bone, aseptically prepared, and draped. Under fluoroscopic or radiographic guidance, a 3.2-mm drill bit is introduced through a stab incision on the medial aspect of the proximal third metatarsal bone, 2 cm distal to the tarsometatarsal joint. The bit is advanced through the third metatarsal bone in an oblique proximolateral direction, penetrating the third metatarsal bone, third tarsal bone and half the thickness of the central tarsal bone. Care is taken not to penetrate the proximal intertarsal joint. The stab incision is closed with a single simple interrupted suture and a light bandage applied before recovery. Horses are stall-confined with daily hand-walking for 10 to 15 minutes until the sutures are removed at 12 days postoperatively. Light riding, including long trotting and straight-line work, is recommended for 30 days before resuming light training.

Prognosis after this procedure has been reported as 62% cure rate based on a client survey 1 year after surgery in 40 cases. The author concluded by stating that fenestration was their treatment of choice for bone spavin compared with other arthrodesis techniques.

ARTHRODESIS OF THE DISTAL TARSAL JOINTS

The goal of distal tarsal arthrodesis is to promote bony union of the joint, which alleviates pain. Because the distal tarsal joints are "low motion," minimal gait abnormalities occur after arthrodesis. Two surgical techniques are discussed in this section: conventional drilling technique previously described and laser-facilitated arthrodesis.

Drilling Technique

The horse is placed under general anesthesia and positioned in dorsal recumbency with the legs suspended, which allows access to the medial aspect of the tarsus. The limb is clipped circumferentially from mid-tibia to mid-cannon bone, aseptically prepared, and draped. A 4- to 5-cm vertical skin incision is centered over the cunean tendon and 3 to 4 cm of the tendon removed. This author uses fluoroscopic guidance to place a 4.0-mm drill bit into the distal intertarsal and tarsometatarsal joints parallel to the joint surface. Three separate drill tracts are made in a fan-shaped pattern to a depth of approximately 3 cm. The goal is to remove cartilage from opposing joint surfaces, allowing bony union to prevent motion of the joint, thus decreasing pain. The fluoroscope allows accurate placement of the drill and decreases overall surgery time. The skin is closed in routine fashion and a light bandage applied before recovery.

Horses are given 2 g of phenylbutazone once a day for the next 5 to 7 days postoperatively, depending on pain

level. Some horses are improved markedly within days after surgery, as a result of previously discussed mechanisms decreasing intraosseous pressure. Horses are stall-confined for 2 weeks, with the legs bandaged until the sutures are removed. Light exercise, including riding or ponying, is recommended for the next 30 days, followed by return to full work if the horse is not in pain. The convalescent period is variable with some horses requiring 6 months to a year to achieve soundness. In a retrospective study of 20 horses, 80% of the horses returned to full function after surgery. The clinical impression of this author is not as favorable. Clients are dissatisfied with the procedure because of the long convalescent period and variable success rate.

Laser-Facilitated Arthrodesis

A full series of radiographs, including a good quality dorsoplantar view, is helpful in planning the surgical approach and predicting prognosis. Radiographic changes with severe periarticular osteophyte formation or excessive mineralization of the joint capsule necessitate modification of the laser procedure to facilitate placement of the laser fiber into the joint and may signify a less favorable prognosis after surgery.

Degenerative joint disease of the proximal intertarsal joint, concurrent with degenerative change of the distal tarsal joints, lends to a guarded prognosis for athletic soundness without periodic medical management of the tarsocrural joint after surgery. In cases of arthritis involving the lower tarsal joints and the proximal intertarsal joint, a contrast arthrogram may be indicated to determine communicability. If the joints communicate, heat and inflammatory components from the laser surgery could affect adversely the proximal intertarsal and tarsocrural joints.

The technique has been performed with the neodymium: yttrium-aluminum-garnet (Nd:YAG), 980-nm diode and holmium lasers, although, the two lasers most commonly used are the 980 nm diode and the Nd:YAG. The horse is placed under general anesthesia in dorsal recumbency and maintained with inhalant anesthetic. The hair is clipped circumferentially from an area extending from the mid-tibia region to the middle of the third metacarpal bone. The area is prepared in routine fashion with a surgical scrub. Performing a final rinse with sterile saline to remove any residual alcohol from the surgical site is important; otherwise, the heat generated by the laser fiber may ignite alcohol vapors on the surface of the skin. Two 18-gauge 1½-inch needles are placed on the dorsomedial aspect of the tarsus into the distal intertarsal and tarsometatarsal joints. Fluoroscopic guidance greatly facilitates the accurate placement of each needle. These needles serve as a parallel guide for the placement of the laser fiber and allow plume to vent out of the joint as laser energy is delivered.

A number 11-scalpel blade is used to make stab incisions at the laser site. A 600-micron conical-tipped laser fiber is introduced into the tarsometatarsal joint through a 3-inch steel 16-gauge needle placed approximately 1 cm from the vent needles on the dorsomedial aspect of the tarsus through the previously made stab incisions into each respective joint. Placement of the fiber can be adjusted

with fluoroscopic guidance to avoid osteophytes or areas of mineralization (Figure 10.12-1). The laser is set to continuous mode at approximately 25 to 30 watts. Short pulses of energy are delivered by cycling the foot pedal until the fiber is felt entering the joint and plume is freely venting out of the 18-gauge needles. Once the fiber is in the joint, the power setting is adjusted to 15 to 20 watts and longer pulses of laser energy are delivered with each cycle of the foot pedal to achieve a constant boil of the synovial fluid. The laser fiber is advanced slowly into the joint to a depth of approximately 1 cm. The goal is to heat the cartilage by boiling the synovial fluid, not to pass the fiber across the joint. Application of the laser is continued until the plume delivers small pieces of charred cartilage. Cold saline solution is constantly dripped over the laser cannula during the procedure to prevent thermal necrosis of the skin. The amount of energy required to produce this effect is usually 800 to 1000 joules per joint. More or less energy must be delivered depending on the size of the joint, the amount of synovial fluid present in the joint, and the degree of existing pathology. The stab incisions are closed with a single simple interrupted monofilament suture and routine tarsal bandages are applied.

Horses are given broad-spectrum antibiotics preoperatively and the following day; 2 g of phenylbutazone are given for 2 to 3 days after surgery, depending on the comfort level of the patient. Bandages are changed every 2 to 3 days until the sutures are removed at 10 days. The horses are stall-confined for 2 weeks after surgery, with 10 to 15 minutes of hand-walking beginning after the first 7 days. After 2 weeks, light exercise, consisting of straight-line trotting or big circles for 10 to 20 minutes, is recommended. This author prefers that operated horses be ponied or ridden as opposed to being lunged. This is continued for 30 days. The next month of exercise involves riding in a straight line or large circles at a trot and lope for 20 to 30 minutes each day. This is followed by a return to light training for an additional 30 days, avoiding sud-



Figure 10.12-1 A 600-micron laser fiber is introduced into the tarsometatarsal joint, using a 3-inch, 16-gauge stainless steel needle positioned approximately 1 cm from the vent needle in that joint.

den stops or tight turns. If the horse is sound at the end of 90 days of controlled exercise, it can be returned to a normal work schedule. Horses with advanced arthritis, manifested by severe periarticular osteophytes, partial joint collapse, or periarticular mineralization may require low doses of phenylbutazone in the initial period of exercise. Stall confinement without return to exercise does not improve chances for future soundness.

The delivery of laser energy into the joint is paramount. Initial short bursts of energy at higher power settings allow the fiber to quickly advance through the joint capsule and become seated in the cartilage. The surgeon knows this has happened once plume or steam is evacuated out of the vent needles. If plume is not seen by the time 50 to 100 joules of energy is delivered, adjustments must be made before continuing. The two most common reasons for this are a plugged vent needle or failure of the laser fiber to enter the joint. Excess energy delivered outside of the joint can lead to partial sloughing of the skin at the laser site or abundant periosteal proliferation on the medial aspect of the tarsus.

To prevent these pitfalls, accurate placement of the vent needles can be confirmed by injection of saline through the laser cannula to confirm communicability with the vent needle and the joint, or the tarsometatarsal joint can be distended from routine injection over the head of the lateral splint bone with saline. On rare occasions, multiple vent needles must be placed at sites distant from the laser portal to achieve adequate release of the plume.

The goal of laser-facilitated arthrodesis is to heat the cartilage and collagen in the surrounding joint capsule by boiling the synovial fluid until it vaporizes. Chondrocytes heated to 50° C die, and collagen heated above 65° C contracts. Chondrocyte death should lead eventually to collapse and fusion of the joint. The "collagen shift" that likely occurs in the joint capsule may provide stability of the joint, decreasing postoperative pain and facilitating fusion.

Data concerning success rates of this procedure using the Nd:YAG laser have been evaluated retrospectively. In

that abstract, 24 horses (all Western discipline horses except one) went from grade 2 or 3 lame to sound. The horse that remained grade 1 lame after laser-assisted arthrodesis was non-weight-bearing (grade 4 lame) before surgery. All Standardbred horses had an increase in earnings postoperatively. This author's clinical impression is that the diode laser is equally effective. Evaluating the usefulness of a procedure by clinical response to therapy is valuable but should be interpreted with caution. Scientific research is under way to look at the effect of the different wavelengths of laser energy and their interactions with tissues in the distal tarsal joints. A variety of parameters outlined in this chapter may be changed in the future based on this research. Compared with the current techniques available, laser facilitated arthrodesis has many advantages. The two most critical to the athletic horse are a short convalescent period and a higher percentage of horses returning to soundness.

Supplemental Readings

- Eastman TG, Bohanon TC, Beeman GM et al: Owner survey on cunean tenectomy as a treatment for bone spavin in performance horses. *Proceedings of the 43rd Annual Meeting of the American Association of Equine Practitioners*, p 121, 1997.
- Edwards GB: Surgical arthrodesis for the treatment of bone spavin in 20 horses. *Equine Vet J* 1982; 14:117-121.
- Hague BA, Guccione A: Clinical impressions of a new technique utilizing a Nd:YAG laser to arthrodesis the distal tarsal joints. *Proceedings of the American College Veterinary Surgeons*, p 9, 2000.
- Markel MD, Hayashi K, Thabit G III: Basic properties of collagen shrinkage and laser-collagen interactions. In McIlwraith CW, Turner AS (eds): *Lasers in the Musculoskeletal System*, Heidelberg, Germany, Springer-Verlag Berlin Heidelberg, 2001.
- McIlwraith CW, Turner AS: Arthrodesis of the distal tarsal joints. In McIlwraith CW, Turner AS (eds): *Equine Surgery: Advanced Techniques*, p 185, Philadelphia, Lea & Febiger, 1987.
- Sonnichsen HV, Svalastoga E: Surgical treatment of bone spavin in the horse. *Equine Pract* 1985; 7:6-9.

CHAPTER 10.13

Postoperative Management of the Orthopedic Patient

JAMES D. LILLICH
Manhattan, Kansas

Little research has been published concerning postoperative management and physical therapy of equine orthopedic patients. Therefore no proof exists that prescribed, aggressive physical therapy of the equine patient alters long-term outcome after surgery. However, assertive physical therapy of the postoperative human athlete has proven successful and enhances long-term outcome. Based on inherent anatomic, behavioral, and surgical procedural differences, harvesting direct applications and drawing conclusions from human postoperative physical therapy may be difficult. Certain guidelines are found within human medicine that may provide veterinary medicine with a fundamental approach to rehabilitation of musculoskeletal injuries. These guidelines consist of balanced pain management, continuous passive motion, and regimented physical exercises for specific injuries and surgical procedures.

Additional factors must be considered when formulating a postoperative plan and rehabilitation protocol for the equine patient. This includes the injured tissue type(s), extent of the tissue damage, healing potential and time of the injured tissue, surgical procedure and approach, type and use of implants, previous injury and/or surgery, and the intended athletic use of the horse. As with human medicine, the result of the rehabilitated equine injury greatly depends on the abilities of individuals responsible for instituting and assessing response to physical therapy in addition to the innate competitive ability of the patient.

PREOPERATIVE AND INTRAOPERATIVE PAIN MANAGEMENT AND MEDICATIONS

Numerous data exist regarding the need for pain management in the treatment of musculoskeletal injuries. Comparatively, the final results of joint reconstructions in humans are greatly influenced by preoperative, intraoperative, and postoperative pain management because rehabilitation can begin sooner if pain is controlled. To provide maximum benefit, pain medications must be administered before the surgical insult.

In the planning of pain control, both systemic and/or local administration should be considered. An additional delivery system would include an epidural catheter. A broad-spectrum or balanced approach to pain management is recommended. Nonsteroidal antiinflammatory medication (phenylbutazone at 2.2 to 4.4 mg/kg), opioid (butorphanol tartate at 0.01 to 0.02 mg/kg), α_2 -agonist,

and local anesthetic (depolarizing) agents should be used either separately or, more effectively, in combination to provide the best pain relief. Recent studies in human beings have shown that regional analgesic techniques improve early rehabilitation over patient-controlled analgesia and are similar to the benefits of continuous epidural infusion.

Other intraoperative medications include sodium hyaluronan and/or corticosteroids. Research documents small and short-term benefits of intraarticular or intrathecal administration of sodium hyaluronan (20 mg), although long-term benefits also may be derived. Intraoperative local administration of corticosteroid (2 to 4 mg of dexamethasone or betamethasone) remains controversial in veterinary medicine. However, intraoperative, intraarticular administration of dexamethasone is relatively common in knee reconstructions in human surgery. Although benefits of pain management may be difficult to detect or appreciate in the acute postoperative phase, analgesic protocols are carried into the postoperative time frame to reduce pain and encourage early postoperative use.

EARLY POSTOPERATIVE PERIOD

The surgical wound must be assessed in the acute postoperative phase. In general, the appearance of the surgical wound within the first few days can be used as a prognostic indicator of the postoperative course. Local inflammation and reaction to suture material is encountered occasionally and is addressed by suture removal and local wound care. Wounds made for the surgical approach are in the repair phase of wound healing within 2 to 3 weeks. Rehabilitation can begin after this time for most simple and uncomplicated musculoskeletal injuries.

The amount of postoperative bandaging is determined by the surgical wound and original injury. Most bandages can be removed or reduced in size within the 2- to 3-week time frame. A light bandage can be maintained and is recommended usually when light exercise is reinstituted. Conversely, heavy bandaging or rigid external coaptation for extended periods should be avoided if an athletic career is anticipated after surgery. Early return to enforced exercise after immobilization can create secondary problems in immobilized, normal tissues including joint capsule and bone. Similar observations have been made in human rehabilitation and rigid immobilization generally is avoided as primary therapy for many human muscu-

loskeletal injuries. Walking is encouraged and prescribed if cast immobilization is used in human ankle injuries. A rule of thumb is to keep the horse confined to stall rest for a period equal to twice that of the immobilization time frame, before reinstitution of light exercise or turnout.

LATE POSTOPERATIVE PERIOD

Formulating and prescribing a detailed exercise plan in addition to requiring reexamination increases owner/trainer compliance. Fundamentally, the approach to rehabilitation should be based on which tissue was damaged and the surgical procedure performed. The healing time and potential of the tissue damaged generally is the rate-limiting step for return to athletic soundness. Instructions for rehabilitation should be based therefore on overcoming the biggest problem first without causing harm to less significant or normal tissue.

Joint Injury

The loss of athletic potential parallels the loss of or damage to weight-bearing articular cartilage. Other tissues that should be assessed are the joint capsule (amount of periarticular fibrosis resulting in reduced range of motion) and the subchondral bone (amount of sclerosis or damage). Lost hyaline cartilage is replaced with fibrocartilage, which is not as biomechanically sound as the original structure. Healing can be manipulated and improved by applying low-grade forces directly after surgery, an approach encapsulated in the practice of continuous passive motion (CPM). CPM is directed at reducing joint stiffness after injury and/or surgery, and primarily reduces bleeding and periarticular edema. Most human literature indicates that CPM has its greatest benefit when started directly after surgery and continued for 72 to 96 hours or until designed rehabilitation protocols can be instituted. A continuous motion device has not been developed for horses, although it is generally thought that movement within the stall may be sufficient to create a desired effect on the healing of a chondral defect.

Current postoperative recommendations for simple (little loss of weight bearing articular cartilage and no evidence of periarticular fibrosis or subchondral bone sclerosis) osteochondral fragmentation removed with arthroscopic techniques would include 30 days of stall rest with hand-walking followed by 30 days of paddock or turn out. Other recommendations include manual flexion and extension of the affected joint for 10 to 15 minutes, two to three times a day during the stall-rest phase (Figure 10.13-1). Flexion and extension exercises increase joint capsule compliance, whereas flexion "holds" (Figure 10.13-2) stretch the muscle fibers of periarticular tendons. Both exercises are prescribed to increase range of motion. Reexamination including radiography may be indicated before the resumption of training.

More complex injuries, defined as severe loss of weight-bearing articular cartilage with periarticular fibrosis and/or subchondral bone sclerosis, need more time to heal. Approximately 4 to 8 months or longer of paddock or turn out rest may be required. During this time, reexamination and medical therapies, including systemic or local sodium

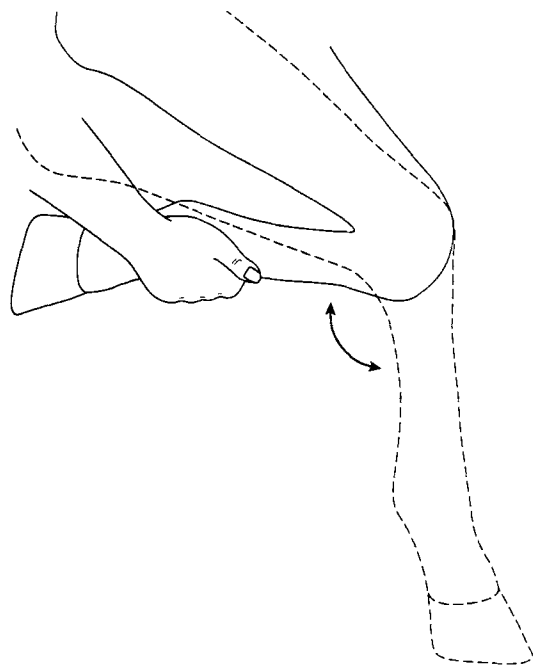


Figure 10.13-1 An example of passive range of motion of the carpal joint.

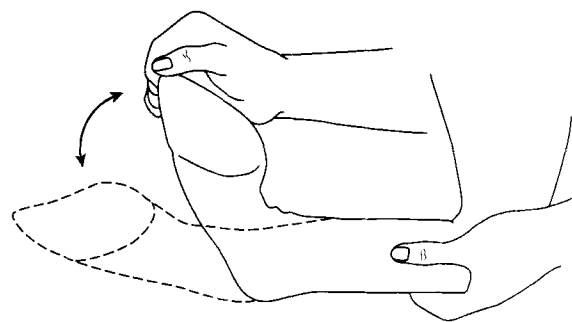


Figure 10.13-2 An example of a "hold" of the fetlock joint.

hyaluronan (20 to 40 mg, given intravenously weekly) or corticosteroid medications, can be prescribed in addition to intramuscular or oral polysulfated glycosaminoglycans (40 mg weekly). Because conflicting data exist regarding the use of these medications, recommendations on their use should be done on an individual basis. Topical therapies also can be recommended to promote pain free, but controlled, use of the injured joint. These therapies include sweats, astringents, ice, and/or hydrotherapy. If exercise is prescribed, it should be limited to low-impact work such as hand-walking, ponying, underwater treadmill, or swimming. Presence of pain, indicated by lameness, is a reliable indicator for altering/adjusting the amount of exercise or work. Reexamination including radiography is prudent before resumption of high-intensity work or training.

Present research trends have focused on returning the damaged joint surface to its original state of hyaline cartilage, be it through resurfacing, gene therapy, mosaicplasty, or grafting. These scientific approaches have shown promise; however, rehabilitation protocols are yet to be investigated to document long-term success.

Tendon and Ligament Injury

Damaged tendon or ligament is slow to heal. Check ligament desmotomy and tendon/ligament splitting are two procedures that may have been performed. Once surgical wounds have healed, the focus of rehabilitation of tendon or ligament relies on medical therapy. Again, lesion severity often dictates the postoperative recommendations.

Medical therapies are directed to encourage intrinsic tendon healing, while discouraging extrinsic tendon healing that leads to adhesion formation and scarring. Therapeutic options include systemic sodium hyaluronan and a variety of topical agents. Clinical reports have documented positive results with topical agents for tendon rehabilitation. In addition, reexamination with ultrasonographic imaging provides valuable information on the status of tendon or ligament healing. Hand-walking can begin within days of surgery and can be continued for 30 to 60 days. From this point, and guided by either ultrasonographic or clinical examination, the horse can be paddock rested or turned out. Present clinical impressions point to a prescribed, controlled exercise protocol, such as ponying, jogging, or light trail riding, providing superior healing results. Complete stall confinement for grade I to II ultrasonographic lesions for extended periods of time has not been rewarding. When treated in this fashion, these lesions tend to change little on ultrasonographic examination and the opportunity to promote intrinsic healing may be missed. Again, ultrasonographic examination usually is required before the resumption of higher-intensity training.

Intralesional therapies, such as corticosteroid or bone marrow aspirates for ligament or tendon injury, have not been tested scientifically for their short- or long-term benefits, nor has the reintroduction of exercise after their use. Although clinical accounts have been favorable, discretion on intralesional therapies should be practiced.

Long Bone Fracture

Normal, healthy bone heals to original strength, and therefore rehabilitation of a fractured bone can be stan-

dardized and results are generally predictable. Typical fractures that can be repaired and the horse returned to athletic function may include stress fractures of the third metacarpus (MCIII), incomplete or nondisplaced condylar fractures of the distal MCIII, and sagittal fractures of the proximal or intermediate phalanx. Again, use of external coaptation should be limited or avoided if possible. Surgical wounds are healed within a few weeks and bandaging may be discontinued after 30 days. Horses can be stall rested and hand-walked for 30 days, followed by 30 days of paddock rest.

Bone takes approximately 4 months to heal completely, but repeat radiographic examination on a monthly basis is needed to assess bone healing. After 60 days, and if supported by radiographic evidence of fracture healing, some implants can be removed if the potential exists for the implant to inhibit athletic performance. Horses can be turned-out for an additional 60 days or placed into low intensity training. Radiographic examination is recommended before returning the horse to full training.

Regardless of the injury, surgically treated horses should be managed by the combined efforts of the referring veterinarian and the surgeon. Insight from both individuals leads to a better outcome for the horse and client.

Supplemental Readings

- Karanikolas M, Swann RA: Current trends in perioperative pain management. *Anesthesiol Clin North Am* 2000; 18:575-599.
- Lane NE, Kaneps AJ, Stover SM et al: Bone mineral density and turnover following forelimb immobilization and recovery in young adult dogs. *Calcif Tissue Int* 1996; 59:401-406.
- O'Driscoll SW, Giori NJ: Continuous passive motion (CPM); theory and principles of clinical application. *J Rehabil Res Dev* 2000; 37:179-188.

CHAPTER 10.14

Bandaging and Casting Techniques

PATRICIA M. HOGAN
Clarksburg, New Jersey

Limb bandages are applied for a variety of reasons on the horse and can be constructed differently to tailor to individual need. The most common indications for a limb bandage are to protect a wound or incision, to control edema or secondary swelling, and to provide some degree of external support and/or immobilization. When properly applied, a limb bandage is effective at achieving the desired goals of protection and/or support; however, a poorly applied bandage can create some serious problems. In addition to the potential ramifications of failing to achieve the purpose of the bandage (i.e., prevent contamination of a wound or incision), a poorly applied bandage can create additional soft tissue problems such as bandage sores, skin necrosis and sloughing, and iatrogenic tendon injury ("bandage bow").

FOOT

The foot can be bandaged effectively with a minimal amount of bandage material. The biggest concern is keeping the bandage and underlying dressing free of moisture and environmental contaminants. For a simple bandage that does not require concussive protection, a roll of conforming gauze can be applied around the hoof, hooking up around the bulbs of the heel, followed by a roll of cohesive bandaging tape (Vetrap Bandaging Tape, 3M Animal Care Products, St. Paul, Minn.). Duct tape then should be applied to the bottom of the foot to protect the bandage from the environment. For a bandage with more concussive protection, a 12-inch by 12-inch section of roll or sheet cotton first can be placed over the bottom of the foot and secured around the hoof with gauze, followed by the cohesive bandage and duct tape. A layer of adhesive tape (Elastikon, Johnson & Johnson Medical, Ethicon Division, Arlington, Tex.) is advisable over the top rim of the bandage to secure it to the skin and to prevent dirt and bedding material from gaining access to the wound area underneath.

With application of duct tape to the foot, making a 10-inch by 10-inch square of overlapping layers is helpful before application of the bandage. This way the bottom of the foot has a thick covering to protect the inner bandage from wear and contamination. The strips are placed in a criss-cross overlapping pattern on a wall or other smooth surface and then peeled off as one large square when ready to use. This square then can be centered on the bottom of the foot, molded up along the sides of the hoof, and se-

cured with several more wraps of tape around the perimeter of the hoof.

LOWER LIMB

The lower limb bandage is the most common type of bandage applied on the horse. The degree of immobilization of the lower limb is dictated by the thickness of the bandage. However, extra padding does not necessarily equate to a stiffer bandage; the key is to apply the padding in separate layers to achieve a greater degree of support. The stiffness or degree of support increases with each additional layer applied.

The lower limb bandage is applied from just below the level of the coronary band up to just below the carpus or tarsus. A greater degree of immobilization of the lower limb is achieved if the bandage is extended to incorporate part of the foot, rather than ending in the mid-pastern. Also less of a problem exists with the lower rim of the bandage rubbing the heel region and causing skin irritation in cases of long-term bandaging. Most commonly, a layer of roll cotton or several combined lengths of sheet cotton is rolled onto the limb and then secured with a layer of gauze followed by a standard roll of cohesive tape. Ideally, the cotton should be $\frac{1}{4}$ inch thick and 3 to 4 feet long to allow for at least four or five turns around the limb. A standard 1-pound roll of cotton can be divided conveniently to make two separate rolls of bandage material.

The bandage typically is applied starting at the bottom of the foot, rolling upwards to the level just below the carpus or tarsus. Care should be taken to ensure that the padding is applied evenly and smoothly and that the overlying gauze is secured with the same degree of tension throughout the entire length of the bandage. Traditionally, the bandage should be applied to the limb in a clockwise fashion to apply tension on the cannon bone and not on the tendons, but the logic of this theory is questionable when applying a thick layer of padding. If more rigid support is required, the bandage can be applied in sequential layers to its desired thickness. Alternatively, a layer of roll cotton can be applied with a gauze overlay, followed by an Army combine secured with another layer of gauze. A layer of adhesive bandage is placed at the top and bottom of the bandage to secure the ends and prevent dirt and bedding material from getting underneath the bandage.

FULL LIMB

Successfully bandaging the full limb can be challenging sometimes, particularly in the hindlimb. The large degree of flexion that occurs at the level of the carpus and tarsus allows for increased slippage of the bandage and bunching of the underlying material. This can result in improper coverage of the wound or incision, and skin irritation or bandage sores along the bony protuberances of the limb. Because of this, the full-limb bandage requires special attention and should be changed routinely every 2 to 3 days.

Some clinicians prefer to “stack” the full-limb bandage and apply it in two stages. The first bandage is applied, centered over the carpus or tarsus, and secured with gauze. Then a separate bandage is applied to the lower limb underneath the first, and in effect it “holds up” the proximal bandage. An overlying layer of cohesive tape then serves to combine the two into a single unit (Figure 10.14-1).

Alternatively, this author prefers to apply the full-limb bandage as one single unit. The roll or sheet cotton is applied, beginning at the level of the fetlock and spiraled up the limb until approximately 4 to 6 inches below the level of the elbow or the stifle. The bandage is then firmly secured with a roll of conforming gauze, followed by two rolls of cohesive bandage material. Several layers of adhesive tape around the top of the bandage secure it to the skin and greatly decrease the tendency of the bandage to slip. Additionally, for a hindlimb bandage, the adhesive tape also is applied in several layers around the tarsus itself to limit the degree of flexion and prevent the point of the

hock from wearing through the bandage (Figure 10.14-2). For the frontlimb, it is helpful to slice a small (2-inch) linear window in the cohesive and gauze layers of the bandage directly over the accessory carpal bone. This releases some of the pressure on this location and decreases the tendency to develop a pressure sore.

CASTS

Casts usually are used for rigid external coaptation of a specific portion of a limb. Casts may be used as a primary treatment for selected fractures and soft tissue injuries or as an adjunctive treatment for stress protection after internal fixation of an injury. Additionally, casts may be indicated for a brief period after wound repair when a limb bandage cannot provide the required degree of immobilization needed for wound healing.

Horses wearing casts require strict stall rest and appetite and body temperature should be noted daily. Horses should be observed walking for several strides on the cast to determine if lameness is increased. Casts technically require minimal aftercare once applied; however, the clinician should be confident that an experienced person will be monitoring the horse and the cast closely every day. Signs of an imminent problem are usually subtle and if gone undetected, the results can be disastrous. The cast should be palpated daily for isolated areas of heat and moisture, indicative of underlying dermal pressure necrosis. The most common locations for this to occur are along the back of the proximal sesamoid bones, the heel bulbs,



Figure 10.14-1 A “stack” full-limb bandage. The first bandage was applied centered over the carpus, and the second bandage was secured underneath the first.



Figure 10.14-2 A full hindlimb bandage. The adhesive tape secured over the tarsus and at the proximal aspect of the bandage helps limit slippage and bunching of the bandage.

and the proximodorsal aspect of the cannon bone. Pressure sores are usually the result of a less-than-perfect fit of the limb within the cast. This may be because the cast is too tight, too loose, or it may have experienced uneven wear along the bottom resulting in shifting of the limb within the cast. Even a cast that is applied perfectly may experience loosening at a later date as a result of resolution of limb swelling associated with the original injury, muscle atrophy, or shifting of underlying padding materials. At the first sign of a problem with wear, serious consideration should be given to removal and replacement of the cast.

Cast Application

The clinician should be well prepared when constructing a cast because once the application is started, little room exists for error in time and judgment. The most commonly used types of casts can be applied in the standing horse using mild sedation with or without the aid of a nose twitch. A full-limb cast is the exception because it is difficult to apply properly and requires general anesthesia.

The limb should be free of dirt and bedding and a light sterile dressing of conforming gauze placed over the wound or incision. A double-layer of orthopedic stockinette is then rolled onto the limb and extended approximately 4 to 6 cm past the anticipated proximal limit of the cast. This material must have no wrinkles or bunching, which could lead to a pressure sore once the cast is applied. If necessary, a thin layer of cast padding then may be applied to the limb. However, minimal padding under the cast is desirable as bulky material compresses over time, altering the fit of the cast. Strips of orthopedic felt are placed around the limb at the proximal aspect of the cast, and around any prominent bony protuberances. This author prefers to routinely apply the felt around the heel bulbs and proximal sesamoids when constructing a half-limb cast and around the accessory carpal bone and the calcaneus when applying a full fore and hindlimb cast, respectively.

Although plaster-based casting material is still used by some clinicians, the preferred cast material is fiberglass. This material offers superior strength and convenience of application, and it is relatively lightweight. Fiberglass casting tape is also porous, which allows for air circulation to the limb underneath the cast. For most casts, the 4-inch or 5-inch rolls of casting tape are the preferred width. Additionally, the use of resin-impregnated foam cast padding (3M Custom Support Foam, 3M Animal Care Products, St. Paul, Minn.) as the first layer has resulted in a better fit and subjectively, a decrease in the incidence and severity of pressure sores. The custom support foam begins to set up on contact with water and its resin bonds with the fiberglass casting tape, resulting in an inner cushion that is incorporated into the cast. This cushion does not shift, is porous, and conforms to the shape of the limb without wrinkling.

Water temperature is an important consideration when any cast is applied. The warmer the water, the faster the cast completes the polymerization process and "cure." Lukewarm is ideal for the inexperienced clinician. However, in the standing sedated horse, time constraints may dictate that an increased temperature is necessary. The rolls of casting tape/foam must be submerged fully and then

any excess water shaken out before application. Gloves are recommended during handling of the cast material.

The custom support foam is applied first and is gently placed on the limb, without tension. It can be overlapped safely in layers in locations that are more susceptible to pressure sores (i.e., proximal cannon bone). The casting tape then should be applied over the foam firmly but not tightly. Starting at the top or the bottom of the limb, the tape is spiraled around the leg, overlapping the previous layer by 50%. The tape should lie down smoothly and without any wrinkles. For half- or full-limb casts, a heel elevation is required. A premade wedge block can be incorporated into the cast or preferably, a roll of 4-inch casting tape is applied partially to the foot and then compressed against the heel. This is then secured to the foot with another roll of 4-inch tape (Figure 10.14-3). Before the last layer is applied, the proximal excess portion of stockinette is pulled down firmly and incorporated into the cast. Last, a form of protection for the bottom of the cast is applied to guard it from excessive wear. This may consist of a strip of rubber from an old tire or a commercial acrylic (Technovit, Jorgenson Laboratories, Inc., Loveland, Colo.).

Foot Cast

Rigid immobilization of the foot is required in selected cases of severe soft tissue injuries, or lacerations involving the heel region and coronary band. Horses generally tolerate a foot or phalangeal cast very well and have few problems with pressure sores. The cast fully encloses the foot and extends up to the mid- to proximal aspect of the pastern region (Figure 10.14-4). Care should be taken to ensure that the palmar/plantar aspect of the pastern and lower fetlock are well protected by the orthopedic felt and that the cast is not too tight in this area.

For this type of cast, the foot is placed flat with no heel elevation. Because the area to cover is small and irregular



Figure 10.14-3 View of the bottom of a half-limb cast at the time of application. A partial roll of 4-inch casting tape has been incorporated into the cast to provide heel support.



Figure 10.14-4 Application of a foot or phalangeal cast. No heel elevation is required, and the proximal aspect of the cast has adequate padding.

in shape, the smaller-width casting tapes (3- or 4-inch) are better suited to allow for an easier change in direction during the application. Usually three to four rolls of casting tape are sufficient for the foot cast. The proximal portion of the cast must be kept covered with adhesive tape throughout its wear period to keep bedding material and soil out of the cast. Most horses can comfortably wear a foot cast for 4 to 6 weeks without incident.

Lower Limb Cast

The lower or half-limb cast is the most commonly applied type of cast in the horse. It is used either as a primary treatment for an injury or as an adjunctive treatment such as in providing external support following internal fixation of a fracture or surgical repair of a soft tissue injury.

Limb position for the half-limb cast is usually with the toe extended forward and supplemental heel support provided. In this manner, the dorsal cortices of the limb are in alignment and less opportunity exists for pressure sores to develop. When applying the cast in the standing horse, the veterinary professional should extend the limb forward, which places the toe on the edge of a board or block. Therefore the limb is in the desired position and the heel region can be included with the initial rolls. Then with an assistant passively flexing the limb at the knee, the last roll of casting tape can be applied to the toe and the heel together. A typical half-limb cast requires four to six rolls of 4-inch or preferably, 5-inch, casting tape. The cast must be extended to just below the carpus or tarsus because the top of the cast is a significant stress concentrator and risk of a catastrophic injury is increased with the cast ending in the middle of a long bone.

Full-Limb Cast

The full-limb cast is the most difficult cast to apply and maintain in the horse, but fortunately it is infrequently required. It always is applied with the horse under general anesthesia and recovery requires some assistance. The basic principles of cast application apply with an emphasis

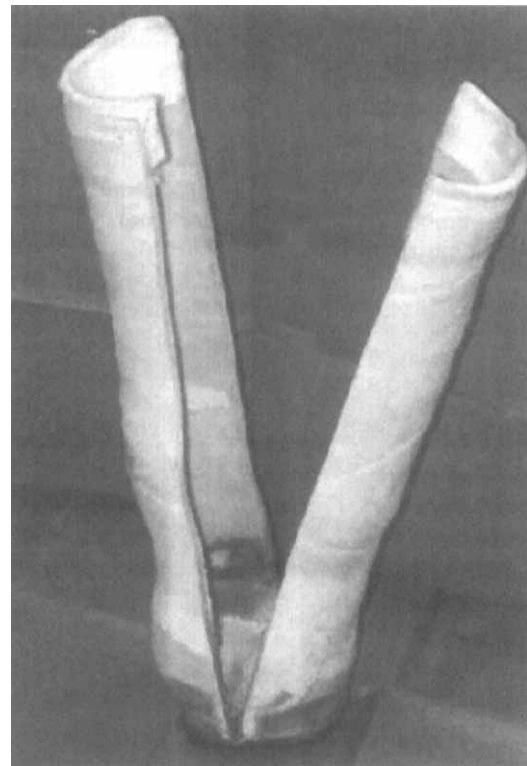


Figure 10.14-5 A bandage cast that has been bivalved and is ready to be reapplied.

on the importance of extending the cast as proximal as possible, terminating immediately distal to the elbow or stifle joint. The proximal aspect of the cast acts as a stress concentrator so that one ending in the mid-diaphyseal region of the radius or tibia may increase the risk of a fracture in recovery. Because of the mechanics of the reciprocal apparatus, horses in full hindlimb casts are prone to rupture or avulsion of the peroneus tertius.

Bandage Cast

The bandage cast offers an alternate form of external coaptation that eliminates some of the restrictions associated with a traditional cast. Basically the bandage cast is a reusable bivalved cast that provides rigid immobilization of the limb yet is amenable to frequent removal and resetting (Figure 10.14-5). The primary advantage of the bandage cast is access to the underlying soft tissues. This is important in cases of severe lacerations, tendon injuries, open synovial structures, and selected orthopedic injuries. Horses seem to tolerate bandage casts well for extended periods of time and cast sores are usually negligible with this method of coaptation because of the amount of padding provided by the bandage material.

A bandage cast can be applied under general anesthesia or in the standing, sedated horse. A sterile dressing is first applied to the limb followed by two or three pieces of thin sheet cotton. This is rolled firmly around the limb and secured with a roll of gauze, followed by a roll of cohesive tape to make a smooth bandage. The foot is included in the bandage. A strip of orthopedic felt is secured around the proximal aspect of the cannon bone. Stockinette is not necessary.

Custom support foam and casting tape is then applied as if to form a traditional cast. The cast is then bivalved at the first dressing change and subsequently replaced each time using duct tape to hold the two halves together.

Supplemental Readings

Bramlage LR, Embertson RM, Libbey CJ: Resin impregnated foam as a cast liner on the distal equine limb. Proceedings of the 37th Annual Convention of the American Association of Equine Practitioners, pp 481-485, 1991.

Hogan PM: How to make a bandage cast and indications for its use. Proceedings of the 46th Annual Convention of the American Association of Equine Practitioners, pp 150-152, 2000.

Murray RC, DeBowes RM: Casting techniques. In Nixon AJ (ed): Equine Fracture Repair, pp 104-113, Philadelphia, WB Saunders, 1996.

Trent AM: Support bandages. In White NA, Moore JN (eds): Current Techniques in Equine Surgery and Lameness, pp 468-476, Philadelphia, WB Saunders, 1998.

CHAPTER 10.15

Intraarticular Corticosteroids

DAVID D. FRISBIE

Fort Collins, Colorado

Since the introduction of intraarticular (IA) corticosteroids as a treatment for joint disease, they have been the standard of many treatment regimes. Although numerous other IA and systemic treatments currently are used in clinical practice, few of these treatments appear to be as potent in the reduction of clinical lameness when compared with IA corticosteroids. As with any medication the use of IA corticosteroids should be considered in light of the risk: benefit: cost ratio. This chapter deals specifically with corticosteroids but a similar ratio should be assigned for all treatment protocols to aid in the approach of clinical cases. The following chapter focuses on three commonly used IA corticosteroids available at the time this chapter was written. Included in this chapter are basic pharmacology, scientific studies associated with each preparation, recommended total body doses, suggestions for postinjection rest period, and regulatory issues in sanctioned events. The goal of this chapter is to present the state-of-the-art in the use of IA corticosteroids.

The use of corticosteroids for the treatment of equine joint disease, in addition to the controversy surrounding the risk benefit ratio of their use have been reported for almost 5 decades in both scientific and lay press. Wheat first reported in 1955 the use of hydrocortisone to treat clinical muscular conditions in 94 horses and in cattle. This report was followed by a series of investigations by Van Pelt and co-workers that evaluated a number of corticosteroid preparations as treatments for a variety of clinical conditions. Mostly favorable results have been reported but all studies were controlled poorly. Few, if any, of the early clinical reports that suggest deleterious effects associated with IA corticosteroid administration have withstood close modern-day scientific scrutiny. Specifically, most of these reports lacked an appropriate control population that would ensure the reported deleterious ef-

fects that occur in corticosteroid treated joints would not have occurred as a natural progression of the disease process.

Extensive reviews dealing with the benefits and controversy surrounding IA corticosteroid administration have been published and serve a good reference if more specific information is sought. Alarming statements such as, "A patient on corticosteroids can walk all the way to the autopsy room" and "A horse can wear a joint surface right down to the bone running on a glucocorticoid-injected joint" exist in the literature despite lack of scientific evidence for these claims. Knowing the historic literature is imperative in addition to critically evaluating future literature for the advancement of equine joint treatments.

PHARMACOLOGY

Modern-day corticosteroids utilized for IA applications are almost exclusively synthetic in nature. These compounds have been formulated to increase the antiinflammatory effects and reduce their influence on water and sodium metabolism common to naturally occurring corticosteroids. These compounds also have been manipulated to control the duration of action, specifically by controlling the lipid or water solubility, which is known to influence duration of action after systemic administration. The lipid solubility can be controlled based on the esters linked to the parent steroid compound.

Scientific studies assessing the IA duration of action are lacking, and most of the published literature is based on systemic administration. Evidence exists that compounds with a slow onset and long duration of action systemically are converted rapidly to an active compound after IA administration. This may or may not decrease the IA duration of action. The thought that "short-acting" and

Custom support foam and casting tape is then applied as if to form a traditional cast. The cast is then bivalved at the first dressing change and subsequently replaced each time using duct tape to hold the two halves together.

Supplemental Readings

Bramlage LR, Embertson RM, Libbey CJ: Resin impregnated foam as a cast liner on the distal equine limb. Proceedings of the 37th Annual Convention of the American Association of Equine Practitioners, pp 481-485, 1991.

Hogan PM: How to make a bandage cast and indications for its use. Proceedings of the 46th Annual Convention of the American Association of Equine Practitioners, pp 150-152, 2000.

Murray RC, DeBowes RM: Casting techniques. In Nixon AJ (ed): Equine Fracture Repair, pp 104-113, Philadelphia, WB Saunders, 1996.

Trent AM: Support bandages. In White NA, Moore JN (eds): Current Techniques in Equine Surgery and Lameness, pp 468-476, Philadelphia, WB Saunders, 1998.

CHAPTER 10.15

Intraarticular Corticosteroids

DAVID D. FRISBIE
Fort Collins, Colorado

Since the introduction of intraarticular (IA) corticosteroids as a treatment for joint disease, they have been the standard of many treatment regimes. Although numerous other IA and systemic treatments currently are used in clinical practice, few of these treatments appear to be as potent in the reduction of clinical lameness when compared with IA corticosteroids. As with any medication the use of IA corticosteroids should be considered in light of the risk: benefit: cost ratio. This chapter deals specifically with corticosteroids but a similar ratio should be assigned for all treatment protocols to aid in the approach of clinical cases. The following chapter focuses on three commonly used IA corticosteroids available at the time this chapter was written. Included in this chapter are basic pharmacology, scientific studies associated with each preparation, recommended total body doses, suggestions for postinjection rest period, and regulatory issues in sanctioned events. The goal of this chapter is to present the state-of-the-art in the use of IA corticosteroids.

The use of corticosteroids for the treatment of equine joint disease, in addition to the controversy surrounding the risk benefit ratio of their use have been reported for almost 5 decades in both scientific and lay press. Wheat first reported in 1955 the use of hydrocortisone to treat clinical muscular conditions in 94 horses and in cattle. This report was followed by a series of investigations by Van Pelt and co-workers that evaluated a number of corticosteroid preparations as treatments for a variety of clinical conditions. Mostly favorable results have been reported but all studies were controlled poorly. Few, if any, of the early clinical reports that suggest deleterious effects associated with IA corticosteroid administration have withstood close modern-day scientific scrutiny. Specifically, most of these reports lacked an appropriate control population that would ensure the reported deleterious ef-

fects that occur in corticosteroid treated joints would not have occurred as a natural progression of the disease process.

Extensive reviews dealing with the benefits and controversy surrounding IA corticosteroid administration have been published and serve a good reference if more specific information is sought. Alarming statements such as, "A patient on corticosteroids can walk all the way to the autopsy room" and "A horse can wear a joint surface right down to the bone running on a glucocorticoid-injected joint" exist in the literature despite lack of scientific evidence for these claims. Knowing the historic literature is imperative in addition to critically evaluating future literature for the advancement of equine joint treatments.

PHARMACOLOGY

Modern-day corticosteroids utilized for IA applications are almost exclusively synthetic in nature. These compounds have been formulated to increase the antiinflammatory effects and reduce their influence on water and sodium metabolism common to naturally occurring corticosteroids. These compounds also have been manipulated to control the duration of action, specifically by controlling the lipid or water solubility, which is known to influence duration of action after systemic administration. The lipid solubility can be controlled based on the esters linked to the parent steroid compound.

Scientific studies assessing the IA duration of action are lacking, and most of the published literature is based on systemic administration. Evidence exists that compounds with a slow onset and long duration of action systemically are converted rapidly to an active compound after IA administration. This may or may not decrease the IA duration of action. The thought that "short-acting" and

“long-acting” corticosteroids must be mixed to obtain a fast and long-acting joint treatment should be questioned. Based in part on suppression of adrenal function and anecdotal reports after IA administration, succinate and phosphate esters presumably are associated with the shortest-acting preparations.

Acetate and acetonide esters are considered less water soluble and more lipid soluble, thus preparations conjugated with these esters are considered of moderate duration. The most lipid and least water-soluble ester is hexacetonide, available as triamcinolone hexacetonide, and considered to be the longest-acting corticosteroid for IA use and is commonly employed in human medicine. Celestone Soluspan is a relatively commonly used corticosteroid in equine practice today. This product is a combination of betamethasone sodium phosphate and betamethasone acetate and was developed to provide fast onset and prolong duration of action. Triamcinolone acetonide (Vetalog), a preparation thought to have a moderate to long duration of action, and methylprednisolone acetate (Depo-Medrol), thought to have one of the longest durations of action, commonly are used in equine practice today.

EQUINE STUDIES

Numerous studies have been conducted both *in vitro* and *in vivo* to assess the effects of corticosteroids on equine tissues. A few studies that followed clinical cases subsequent to IA corticosteroid use also have been published. Many of these studies have been conducted on normal tissues, whether it was normal articular cartilage that was harvested and used for *in vitro* studies or normal equine joints in *in vivo* studies. Recently published literature suggests that normal joint tissue reacts differently than diseased or stressed joint tissue. Specifically, some detrimental effects associated with corticosteroid administration on normal tissue were not observed when a similar dose was administered to diseased or stressed tissue. This implies caution should be exercised when interpreting studies conducted on normal joint tissues and drawing conclusions on the clinical use of corticosteroids especially because the clinical indication for IA corticosteroids is on diseased joint tissue.

Betamethasone

Betamethasone products have not been the focus of many equine studies. The inconsistent availability of veterinary and human preparations may have contributed to this. Currently Celestone Soluspan is the only commercially licensed betamethasone compound available, although compounding pharmacies historically have been able to supply similar products (3 mg betamethasone sodium phosphate and 3 mg betamethasone acetate).

One noteworthy study has been completed in horses using Betavet. This study was one of the first to use an arthroscopically created osteochondral fragment to emulate joint disease. Although the model was in an early stage of development and the pathology induced in the model did not reach statistically significant levels, no significant detrimental effects of Betavet were observed at two 15-mg doses 14 days apart. No significantly beneficial effects were confirmed in this study either, which in light

of the anecdotal benefit of this medication clinically suggested some contribution of the model to the lack of significant findings. Despite the lack of an overwhelming number of equine studies, betamethasone products still are used clinically when a relatively short acting IA steroid is needed.

Methylprednisolone Acetate

One of the first experimental studies conducted in horses used methylprednisolone acetate (MPA). This study used an arthrotomy incision to create experimentally an osteochondral fragment as a model of joint disease. The fragment was of a size that closely resembled a slab fracture, which represented a severe form of joint disease that is not often treated with corticosteroids alone if the goal was long-term athletic performance. A relatively high dose and frequent dosing regime also was employed in this study, with 120 mg of MPA administered biweekly for four treatments superimposed on strenuous exercise. In this study, only one horse served as a control. Although this study was one of the first to begin to address the use of corticosteroids in diseased joints, the model does not represent accurately the use of corticosteroids in modern-day equine practice, and one control horse was not adequate to provide an accurate representation of the effects produced by the large fragment alone. Detrimental effects demonstrated in this study should be interpreted with these factors in mind.

More recently Depo-Medrol was evaluated in a revised arthroscopic osteochondral fragment model that used a fragment size more representative of most clinical cases. Further evaluation and refinement of this model have led this author to believe that it closely mimics clinical synovitis and secondary osteoarthritis (OA) observed in equine joint disease but does not recreate the bone pathology observed in clinical cases of osteochondral fragmentation. This model appears to be valid to assess joint medications based on comparisons of experimental results to the anecdotal clinical reports associated with medications tested using the model. Depo-Medrol assessed at a 100-mg dose administered twice, 14 days apart, 2 weeks after fragment creation showed both positive and potentially negative results. The clinical improvement in lameness was not statistically significant when compared with control horses. Other parameters of joint pain, such as synovial fluid prostaglandin E₂ levels, were significantly improved. Microscopic improvement in the synovial membrane also was demonstrated with the administration of Depo-Medrol but microscopic and biochemical tests on the articular cartilage demonstrated potentially detrimental results. This study also confirmed the finding of “red, dry joints” previously reported in association with MPA administration. In light of current literature, the use of Depo-Medrol alone should be considered carefully, especially in high-motion joints in which cartilage preservation is paramount and in horses in which the joints are subjected to a rapid return to athletic endeavors.

Triamcinolone Acetonide

Using the same arthroscopic osteochondral fragment model describe previously, Vetalog was evaluated using

two 12-mg doses administered 14 days apart. Significant improvement in clinical lameness, microscopic synovial membrane, and articular cartilage parameters, in addition to improved biochemical parameters in both the synovial fluid and cartilage were demonstrated in the Vetalog compared with the placebo-treated horses. This was one of the first *in vivo* studies conducted in the horse that suggested a chondroprotective effect of a corticosteroid preparation. The contrast in results between Vetalog and Depo-Medrol are noteworthy. The results of the Vetalog study has spawned some clinicians to use preferentially a triamcinolone-based product alone or in combination with other medications in high-motion joints when the joint will be subjected to a rapid return to athletic endeavors.

In summary, based on the scientific literature published at the time of this chapter, the use of either betamethasone or triamcinolone products in high-motion joints is recommended. Clinically these products often are combined with other medications such as sodium hyaluronate with anecdotally good responses. Methylprednisolone products certainly still have a place in equine practice given the long duration of action subsequent to IA administration. The dose, frequency, postinjection exercise protocol, and anatomic location of their use should be considered because of potentially detrimental effects suggested in current literature.

RECOMMENDED DOSES

A few studies have attempted to assess the optimal dose of corticosteroids, and some have even been performed on equine tissues; however, most of these studies have been *in vitro*. Some have suggested that a lower dose of corticosteroids may obtain the beneficial effects without any detrimental effects. Further work on this theory has yielded some conflicting results, with a recent study observing doses close to those used clinically being required to stop cartilage degradation by a major catabolic mediator, interleukin-1. Currently a dose in the range of 6 to 15 mg for betamethasone, 6 to 12 mg for triamcinolone acetate, or 60 to 100 mg for methylprednisolone acetate is recommended per joint. The frequency of injection is limited to the minimum number needed to achieve soundness. If repeat injections are required, attempts to rule out other significant pathology should be explored completely. The frequency of injections somewhat depend on the specific joint and level and degree of work. For example, an annual distal hock joint injection in a working Quarter Horse or a limited number of bimonthly fetlock injections during the strenuous period of a jumping circuit may constitute a reasonable injection frequency.

In practice, corticosteroids often are combined with sodium hyaluronate. Although some scientific evidence supports this combination, little published work in this area has been completed. This combination therapy has received much anecdotal support because of assumed joint normalization effects of sodium hyaluronate and the potent antiinflammatory properties of corticosteroid as the basis for the combination. A dose of 10 to 20 mg of sodium hyaluronate combined with the previously listed corticosteroid dose is used commonly. Even though this combination does not have overwhelming published evi-

dence of efficacy the lack of reported deleterious effects supports its use.

Although no scientific studies have proven a causal link of IA corticosteroid administration and laminitis, various compounding factors appear to provide some degree of association between the two events. Therefore all corticosteroids may possess the ability to induce laminitis and the therapeutic index may not be the same for all preparations. Anecdotal reports certainly suggest a narrower therapeutic index with Vetalog as compared with Depo-Medrol and Betavet/Celestone Soluspan when it comes to laminitis as a secondary complication with IA administration. It has been suggested that the total body dose of Vetalog not exceed 18 mg, Depo-Medrol 200 mg and Betavet 30 mg. Although these numbers are based on some fact and some fiction, one of the main goals is to eliminate corticosteroid-induced laminitis and these numbers have been a good rule of thumb for many practitioners.

Postinjection Exercise Protocol

To date, controlled studies have failed to prove that postinjection exercise leads to macroscopic joint tissue degeneration even when doses and frequencies of administration exceed typical clinical recommendations. This suggests that corticosteroids are relatively safe even with ongoing exercise. This outlook is relatively simplistic, however. A more conservative approach is most likely prudent because corticosteroids have been shown to affect the metabolism of articular cartilage, especially normal cartilage. Although the previous sections have pointed out that not all corticosteroids have similar detrimental effects, negatively altered metabolism does occur with some corticosteroids and is thought to contribute to degeneration of the joint surface in the face of strenuous exercise. Unfortunately, to date the level of abnormal metabolism that leads to long-term pathology has not been defined. Most studies assessing the time for cartilage metabolism to return to normal suggest this period is about 4 to 8 weeks after the last dose. Similarly, a study looking at alterations in normal articular cartilage biomechanics after corticosteroid administration combined with strenuous exercise suggested that subclinical changes would persist for at least a month. Published work in dogs does suggest that some level of "normal" loading is beneficial for cartilage metabolism after corticosteroid administration.

No definitive length of postinjection exercise has been documented. Therefore various factors should be used to determine an individual's protocol, including the client's level of conservativeness. One factor to consider is owner/trainer compliance of a 4- to 8-week rest period, which is usually difficult to achieve. IA corticosteroids most likely have less detrimental effects when administered in an abnormal joint environment. Because some level of exercise or loading has been shown to increase the cartilage metabolism, this author uses a 7- to 10-day stall/run confinement, followed by a week of slow return to full work as a working postinjection protocol. This protocol should be used as a guideline and may need adjustments as further information is gained. However, more accelerated protocols have been advocated by some clinicians without apparent detrimental effects.

REGULATORY ISSUES ASSOCIATED WITH COMPETING HORSES

Three governing bodies oversee most of the sanctioned equine competition in the United States: American Horse Shows Association (AHSA), Federation Equestre Internationale (FEI), and the Association of Racing Commissioners International (ARCI). Although stated in different terms, these organizations attempt to limit drug use for the purpose of altering a horse's performance while competing in sanctioned events. Based on this intent, use of IA corticosteroids may not be in complete compliance with drug policies drafted by these organizations. This necessitates that the equine practitioner be aware of the period of time a horse will test positive for corticosteroids after their administration, or the "withholding times."

In Canada, Australia, and Western Europe, withholding times are based on standardized testing methods that help eliminate the interlaboratory variability based on differences in detection methods. These times are published setting up loose guidelines for the equine practitioners. Unfortunately such a reference for IA corticosteroids does not exist in the United States. Veterinary practitioners always should consult the governing body for the latest information regarding withholding times, but some general guidelines based on commonly employed detection methods in use at the time of this publication are as follows:

- Methylprednisolone acetate is detectable for about 7 to 10 days after a single 200-mg IA injection, although detection has been reported for up to 44 days in urine using sensitive detection methods.
- Triamcinolone acetonide is detectable typically for about 9 days after IA administration of 30 mg (note this is greater than the recommended total body dose).
- No published studies are available regarding the detection time of betamethasone products after IA administration; however, extrapolating for published detection times after systemic administration suggest withholding times are probably in the range of 4 to 7 days.

The suggested withholding times should be obtained from the laboratory responsible for the drug testing of a

specific event. In addition, knowing how stringently the governing body regulates the use of corticosteroids is also useful. As a general rule the AHSA is less stringent for most events (with the exception of AQHA sanctioned competitions) compared with the ARCI or FEI. Strict adherence to withholding times is important when a horse is competing in an ARCI or FEI event.

In summary, IA corticosteroids are one of the most commonly used medications for the treatment of equine joint disease, and with careful use and adherence to suggested guidelines they can be a safe and effective way to manage a difficult disease process in the horse.

Supplemental Readings

- Autefage AM, Alvinerie M, Toutain PL et al: Synovial fluid and plasma kinetics of methylprednisolone and methylprednisolone acetate in horses following intra-articular administration of methylprednisolone acetate. *Equine Vet J* 1986; 18:193-198.
- Foland JW, McIlwraith CW, Trotter GW et al: Effect of betamethasone and exercise on equine carpal joints with osteochondral fragments. *Vet Surg* 1994; 23:369-376.
- Frisbie DD, Kawcak CE, Baxter GM et al: The effects of 6-alpha methylprednisolone acetate on an in vivo equine osteochondral fragment exercise model. *Am J Vet Res* 1998; 12:1619-1628.
- Frisbie DD, Kawcak CE, Trotter GW et al: The effects of triamcinolone acetate on an *in vivo* equine osteochondral fragment exercise model. *Equine Vet J* 1997; 29(5):349-359.
- Kawcak CE, Norrdin RW, Frisbie DD et al: Effects of osteochondral fragmentation and intra-articular triamcinolone acetonide treatment on subchondral bone in the equine carpus. *Equine Vet J* 1998; 30(1): 66-71.
- McIlwraith CW: Intra-articular and systemic medications for the treatment of equine joint disease. *Am Assoc Equine Pract* 1996; 42:101-125.
- Tobin T: Steroidal anti-inflammatory agents: the corticosteroids and ACTH. In Tobin T: *Drugs in the Performance Horse*, pp 132-148, Springfield, Ill, Charles C Thomas, 1981.
- Trotter GW: Intra-articular corticosteroids. In McIlwraith CW, Trotter GW (eds): *Joint Disease in the Horse*, pp 237-256, Philadelphia, WB Saunders, 1996.

CHAPTER 10.16

Additional Intraarticular Therapies

LISA A. FORTIER
Ithaca, New York

Administration of medications directly into the articular environment is intended to provide high levels of therapeutic compounds to restore the joint environment, halt the progression of cartilage damage, and decrease inflammation in both the cartilage and synovium. The number of individual joints medicated at any one time depends on the temperament of the horse, time required to aseptically prepare and inject multiple joints, and most importantly, the cost of medicating multiple joints. When the lameness is apparently the result of generalized soreness and cannot be isolated to a specific joint, then intramuscular (IM) administration of polysulfated glycosaminoglycans (PSGAG; Adequan) or intravenous administration of hyaluronan (Legend) would be preferred given the presumption that all joints would be medicated, but to a lesser degree than if compounds were injected directly into the joint. Two common scenarios warrant intramuscular/intravenous therapy. First would be the young racehorse in training that develops multiple joint idiopathic synovitis. Second would be the elderly stallion or show horse that is sore all over but not particularly lame in any one limb.

HYALURONAN

Hyaluronan (HA) is present within articular cartilage, where it is synthesized by chondrocytes, and in the synovial fluid, where it is synthesized by type B synoviocytes. Hyaluronan can exist as hyaluronic acid, sodium hyaluronate, or hyaluronate depending on the environment in which it is found, and all terms are used interchangeably. In osteoarthritis (OA) the molecular weight and concentration of HA are diminished to one half to one third of their normal values. This has given rise to the concept of viscosupplementation.

In both articular cartilage and in synovial fluid, HA plays a critical role in maintenance of joint homeostasis. In articular cartilage, HA provides the backbone for proteoglycan aggregation, which is necessary for maintaining the compressive stiffness of articular cartilage. Hyaluronan imparts the viscoelastic nature to synovial fluid, which means that at low shear rates, it behaves as a viscous solution, and at high shear rates it is elastic. In synovial fluid HA also lubricates the synovial membrane/cartilage interface (boundary lubrication) and physically excludes active inflammatory components and leukocytes from the joint cavity, a mechanism known as *steric exclusion*. Hyaluronan

has additional direct antiinflammatory effects and has been shown to decrease tendon adhesions and fibroblastic pannus formation in osteoarthritic joints.

Given these various mechanisms of action, HA may be of benefit in treating horses with synovitis but without overt osteoarthritis as characterized by full-thickness cartilage erosions or osteophytes. Administration of HA into joints with severe OA may be of some benefit in reduction of the secondary synovitis, which may slow the progression of OA. It also may aid in lubrication of the joint capsule, but it does not heal cartilage in severe OA. These patients have a far less apparent clinical response to HA administration.

The abilities of HA to function as a viscoelastic fluid and to sterically hinder inflammatory components are directly dependent on the molecular weight and concentration of HA. This concept should be kept in mind when choosing from the assorted available preparations of HA available for use (Table 10.16-1). Similarly, the molecular weight of equine synovial fluid HA has been reported to range between 2 and 3 million daltons, whereas the reported concentration of HA ranges between 0.33 and 1.5 mg/ml.

Typically, molecular weight and price are correlated directly. Currently, the most commonly used and least expensive HA product used in racehorses is MAP-5 (Bioniche Teo, Inverin, Ireland). Even though it is not approved for treatment of joint disease; MAP-5 is approved for embryo preservation. The lower-molecular-weight HA products, such as MAP-5, may be efficacious in a typical synovitis or mild OA case. However, in cases in which synovial or tendinous adhesions are to be prevented, the high molecular weight preparations are recommended because of their increased efficacy and longer duration of action.

The various HA products have excellent safety profiles. Joint flares have been reported to occur in approximately 5% of injections. Joint flares can be difficult to distinguish from joint infection in the first 24 hours and may require active treatment such as joint lavage, analgesics, nonsteroidal antiinflammatory drug treatment, and precautionary antibiotic administration. The clinical presentation of joint flares is typically milder than a joint infection with regard to joint swelling, lameness, and synovial white blood cell count. In addition, joint flares are self-limiting and usually resolve within 24 hours.

The dosing routine for hyaluronan in horses has been arrived at based on clinical impressions and each horse's clinical response to HA administration varies. When administered for idiopathic synovitis, HA typically is

Table 10.16-1
Commercially Available Preparations of Hyaluronic Acid

Product	Manufacturer	Concentration (mg HA/ml)	Molecular Weight (daltons)*	Recommended Dose†	Approximate Cost/20mg (\$)
Hylartin-V	Pharmacia	10	2.85×10^6	20 mg	45.00
Hyalovet	Fort Dodge	10	0.81×10^6	20 mg	30.00
MAP-5	Bioniche Teo	10	0.76×10^6	NA‡	15.00
Legend	Bayer	10	0.36×10^6	20 mg	25.00

*Data from Uden PC, Lavoie LM: Laboratory evaluation of commercial hyaluronate sodium products.

J Equine Vet Sci 1997; 17(3):123-125.

†Manufacturer recommended dose for small joint, such as fetlock or carpus.

‡Not approved for use in joint disease.

injected into the joint (IA) every 3 to 6 weeks for three injections. No rest period is required after HA administration. Many horses do not require more than one injection, whereas others appear to do best when HA is administered as a matter of routine maintenance every 6 to 8 weeks. Unlike corticosteroid injections, repeated HA injections do not result in progressive cartilage and joint destruction.

Large blinded, randomized clinical trials in humans suggest that HA supplementation provides a similar level of pain relief as corticosteroids and does so for several months longer. However, the onset of action is slower for HA, typically 2 to 4 weeks as compared with 3 to 7 days for corticosteroids. These findings led to the common practice of combined administration of a short-acting corticosteroid with HA. HA administration has been shown to diminish the well-known degradative effects of corticosteroids on articular cartilage; however, the routine use of corticosteroids with HA is discouraged. Combination HA/corticosteroid therapy is recommended when treating synovitis that is minimally responsive to HA alone, or when treating the coffin joint, which does not appear to respond clinically as well to HA therapy as other joints. A typical combination for coffin joint injection would consist of 20 mg Hylartin-V and 20 mg methylprednisolone acetate.

The manufacturer recommended dose for each HA product is used for most joints primarily because the products are packaged individually in these amounts. The manufacturer recommended doses are based on use in a fetlock or carpus. Therefore when HA is used in a large joint, such as a stifle, the veterinary practitioner probably should administer a double dose. When HA is administered to prevent adhesions, such as after tenoscopic surgery or repair of an intraarticular fracture, then HA obviously would be most beneficial in the immediate postoperative period. In this scenario, HA is administered immediately postoperatively and again in 7 to 10 days.

POLYSULFATED GLYCOSAMINOGLYCAN

The commercially available form of polysulfated glycosaminoglycan (PSGAG) in North America is Adequan. PSGAG is capable of stimulating chondrocyte metabolic activity while concurrently inhibiting the effects of many enzymes involved in cartilage breakdown. PSGAG also

stimulates HA synthesis by the synovial membrane and has antiinflammatory and analgesic properties. These beneficial effects on cartilage metabolism have been demonstrated in numerous species in both *in vitro* and *in vivo* studies and in multiple types of naturally occurring and experimental joint diseases.

Despite extensive research, the exact mechanisms of action of PSGAG remain unknown. The glycosaminoglycan (GAG) molecule present in PSGAG is chondroitin sulfate, which is chemically modified to have a very high negative charge. Through the negatively charged sulfate groups, the chondroitin sulfate GAGs are able to bind to cartilage matrix molecules including collagen, proteoglycans, and noncollagenous proteins. This binding is thought to be at least in part responsible for the mechanism of action of PSGAG.

Originally, PSGAG was designed and evaluated for IA administration. When used IA, PSGAG was administered at a dose of 250 mg weekly for a minimum of 3 weeks with good clinical results. However, joint infection is potentiated by the administration of PSGAG through inhibition of both the classic and alternative pathways of complement activity. To circumvent potentially devastating iatrogenic IA infections, IM administration of PSGAG was evaluated. After administration of 500 mg PSGAG IM, therapeutic levels of PSGAG were found in multiple joints for up to 12 hours. It currently is recommended that PSGAG be administered IM at 500 mg every 3 to 5 days for a minimum of five treatments. It is certainly safest to administer PSGAG IM; however, if one is going to administer PSGAG IA, then an aminoglycoside (e.g., 250 mg amikacin) should be injected concurrently. Although no studies have been performed to determine the effects of amikacin injection on PSGAG activity, clinical responses do not appear to decline.

PSGAG-like products are available for use. When evaluating these products for potential efficacy, the veterinary practitioner should attempt to learn if the chemical composition of the comparison product is truly similar to Adequan. The most striking differences found are in the type of glycosaminoglycan and in the degree of sulfation present. As stated above, Adequan is essentially chondroitin sulfate that has been highly sulfated through chemical manipulations. Several products are on the market that claim to be polysulfated, yet when tested have about one-

third the amount of sulfate of Adequan and essentially are solutions of unmodified chondroitin sulfate. Furthermore, none of these products are approved for use in the treatment of osteoarthritis. Extensive research supports the use of Adequan and these results will likely change when a different compound is administered.

SUPEROXIDE DISMUTASE

Superoxide dismutases (SODs) are metalloproteins marketed as free radical scavengers with antiinflammatory effects. The generic name for SOD is *orgotein*, and in North America, SOD is sold under the name *Palosein*. SOD is not commonly used in practice and few research or clinical reports investigate its use. Controlled studies performed either by investigating clinical response or in *in vitro* cartilage studies do not indicate any benefit of SOD administration.

PENTOSAN POLYSULFATE

Pentosan polysulfate (PPS) was used initially in humans as an anticoagulant, then as an antiinflammatory, and most recently as the major treatment for interstitial cystitis. PPS is made from beechwood shaving and is inexpensive. Both the sodium (NaPPS) and calcium (CaPPS) forms exhibit a wide range of pharmacologic activities with CaPPS reported to have greater bioavailability than NaPPS. PPS stimulates chondrocytes to synthesize new cartilage matrix and inhibits multiple degradative enzymes and inflammatory mediators, thereby attenuating catabolic events responsible for the loss of cartilage matrix in OA joints. Substantial evidence demonstrates that PPS can simulate the synthesis of HA by synoviocytes and that PPS stimulates the release of tissue plasminogen activator, consequently increasing fibrinolysis with resulting improvement in synovial membrane and subchondral blood flow. Presently, NaPPS is available in Australia and several European communities under the brand name of Cartrophen for treatment of equine and canine OA. In horses, CaPPS was found to reduce lameness postracing when administered at a dose of 2 mg/kg intramuscularly once weekly for 4 weeks. In North America, it is available in Canada (Arthroparm Pharmaceuticals, Inc., Ottawa, Ontario, Canada) for treatment of dog OA.

ATROPINE

The antimuscarinic agent, atropine sulfate, has been used to reduce the clinical signs of idiopathic synovitis. The

mechanism by which atropine reduces synovial effusion is not known. It is most commonly used in the tibiotarsal and fetlock joints at a dose of 6 to 8 mg/joint with 8 mg triamcinolone acetate and 250 mg amikacin. The majority of horses treated with atropine have been treated previously with and were unresponsive to corticosteroid therapy. Needing to treat more than two to three joints at a time is rare, so the total horse dose does not typically exceed 20 mg of atropine. Results should be seen within 2 weeks. Because of the parasympatholytic effects, the veterinary professional always should be cognitive of potential gastrointestinal stasis. It is advisable to stay below the recommended total horse dose, perhaps even half that for draft breeds and Miniature Horses.

Supplemental Readings

- Balazs EA, Denlinger JL: Viscosupplementation: a new concept in the treatment of osteoarthritis. *J Rheumatol* 1993; 20:3-9.
- Fuller CJ, Ghosh P, Barr ARS: Plasma and synovial fluid concentrations of calcium pentosan polysulphate achieved in the horse following intramuscular injection. *Equine Vet J* 2002; 34:61-64.
- Guidolin DD, Pasquali Ronchetti I, Lini E et al: Morphological analysis of articular cartilage biopsies from a randomized, clinical study comparing the effects of 500-730 kDa sodium hyaluronate (Hyalgan) and methylprednisolone acetate on primary osteoarthritis of the knee. *Osteoarthritis Cartilage* 2001; 9:371-381.
- Gustafson SE, McIlwraith CW, Jones RL: Comparison of the effect of polysulfated glycosaminoglycan, corticosteroids, and sodium hyaluronate in the potentiation of a subinfective dose of *Staphylococcus aureus* in the midcarpal joint of horses. *Am J Vet Res* 1989; 50:2014-2017.
- Haugland LM, Collier MA, DeBault LE et al: ³H-PSGAG concentration in the synovial fluid of the equine antebrachiocondylar, metacarpophalangeal, coronopedal and tibiotarsal joints following a 500 mg IM injection. *J Equine Vet Sci* 1995; 15:274-278.
- Howard RD, McIlwraith CW: Hyaluronan and its use in the treatment of equine joint disease. In McIlwraith CW, Trotter GW (eds): *Joint Disease in the Horse*, Philadelphia, WB Saunders, 1996.
- Kirwan J: Is there a place for intra-articular hyaluronate in osteoarthritis of the knee? *The Knee* 2001; 8:93-101.
- Tulamo RM, Heiskanen T, Salonen M: Concentration and molecular weight distribution of hyaluronate in synovial fluid from clinically normal horses and horses with diseased joints. *Am J Vet Res* 1994; 55:710-715.

CHAPTER 10.17

Systemic Therapies for Joint Disease

TROY N. TRUMBLE
CHRISTOPHER E. KAWCAK
Fort Collins, Colorado

Many types of therapies are available for the treatment of joint disease in the horse, some of which have been objectively proven beneficial, and others that have been shown anecdotally to be beneficial. This chapter discusses systemic therapies available for the treatment of joint disease in the horse.

PATHOBIOLOGY OF JOINT DISEASE

The pathogenesis of osteoarthritis in the horse is a complex, dynamic process. It involves the interaction of all of the components of the joint. In a normal joint, the matrix components of articular cartilage in addition to subchondral bone routinely are turned over. Bone is always in a constant flux to respond to changing loads. Cartilage is turned over more slowly, with aggrecan turning over more rapidly than type II collagen. This normal turnover is performed by a balance between the actions of degradative enzymes (matrix metalloproteinases, aggrecanase, serine proteinases, etc.) and inflammatory mediators (interleukin-1 α , interleukin-1 β , tumor necrosis factor α , etc.). When trauma occurs within the joint, the turnover process reaches a hypermetabolic state. Initially, synthesis of aggrecan and type II collagen, in addition to type I collagen in the bone tries to keep up with the degradation of these matrix components. Over time, however, with continued trauma, synthesis cannot keep up with degradation, and joint catabolism occurs.

TREATMENT PRINCIPLES

Selection of an efficacious treatment regimen for horses with osteoarthritis is challenging and often involves a combination of pharmacologic and nonpharmacologic therapies. Ideally, the goals of any systemic therapy are to return the joint environment back to normal and to prevent osteoarthritis. One of the important components of any therapy is pain relief, which may include the reduction in inflammation. Therefore an important component of systemic therapy is removal of inciting causes of inflammation. This includes removal of osteochondral fragments, diagnosis of intraarticular ligamentous injuries, in addition to stabilization of intraarticular fractures. In the treatment of traumatic joint disease, pain relief that allows the horse to return to performance must be a balance of

timely and accurate use of systemic therapies in addition to local or intraarticular therapies.

NONSTEROIDAL ANTIINFLAMMATORY DRUGS

Nonsteroidal antiinflammatory drugs (NSAIDs) inhibit the conversion of arachidonic acid into prostaglandins and thromboxanes. All NSAIDs inhibit cyclooxygenase activity to varying degrees. This is most likely the result of differential inhibition of either constitutive (COX-1) or inducible (COX-2) forms of cyclooxygenase. COX-1 is responsible for production of prostaglandins important for normal physiologic functions, whereas COX-2 is induced by bacterial lipopolysaccharide and cytokines and most likely plays an important role in inflammation. The actions of NSAIDs against COX-1 explain some of the major side effects of NSAID administration, for example, gastric ulceration. Aspirin, as an example, more potently inhibits COX-1 than COX-2, thereby presumably affecting normal physiologic functions more so than inflammatory functions. NSAIDs also have a variable effect on proteoglycan synthesis. A number of NSAIDs are thought to inhibit proteoglycan synthesis, whereas some actually increase synthesis. Therefore the veterinary practitioner should weigh the potential for deleterious effects on the articular cartilage against the benefit of the antiinflammatory effects of the NSAID. However, this effect of NSAIDs on proteoglycan synthesis is minimal when compared with the benefits of its anticatabolic effects.

Phenylbutazone

Phenylbutazone is likely most useful in situations where prostaglandin E₂ (PGE₂) production plays the major role in inflammation. PGE₂ has a major role in pain production, in part by amplification of the pain producing properties of histamine and bradykinin, and has been shown to play a role in equine joint disease. Phenylbutazone therefore can exert its analgesic effects by inhibiting PGE₂ production in peripheral sites of inflammation. It apparently does not have any effect on the proteoglycan synthesis. The half-life of phenylbutazone is 4 to 8 hours but extends to 24 hours in inflammatory exudate. Because of this prolonged duration of action in the exudates,

phenylbutazone can be administered successfully once a day at a dose of 4.4 mg/kg. Another common practice is to administer the drug twice a day at 2.2 mg/kg. Administration is either via oral route or intravenously; however, care must be taken when administering phenylbutazone intravenously because perivascular injection causes tissue sloughing.

Clinically, phenylbutazone is probably the best overall systemic therapeutic agent available to the equine practitioner for treatment of joint disease. The majority of mild lamenesses in the performance horse can be managed successfully with phenylbutazone. In the authors' opinion, phenylbutazone is useful for cases of synovitis, capsulitis, and mild sprains. In experimental models of synovitis, phenylbutazone is superior to ketoprofen in regard to reducing lameness, synovial fluid volume, and synovial fluid PGE₂ levels. When dealing with more debilitating injuries to the joint such as destabilization or established osteoarthritis, phenylbutazone is best used in periods of acute flare-ups of the inflammatory process. Prolonged administration should be avoided if possible. However, sometimes the effects of no phenylbutazone administration are worse than the potential toxicity of the drug.

Each horse responds differently to the 4.4 mg/kg daily dose of phenylbutazone. This partly depends on the health, age, and hydration status of the horse. Young, debilitated, or dehydrated horses are at the most risk for toxicity because of reduced efficiency of metabolism and elimination. Unfortunately, these patients often have the greatest need for antiinflammatory medication. Presumably, the most common phenylbutazone-related toxicities in the horse are related to the fact that phenylbutazone is a more potent inhibitor of COX-1 than COX-2. Common toxicities include ulceration of the glandular portion of the stomach and of the right dorsal large colon, renal papillary necrosis, and vascular thrombosis. High doses (15 to 30 mg/kg/day) have been shown to cause anorexia, depression, and death within 4 to 7 days. Clinically, phenylbutazone should be administered for only the length of time that it is absolutely necessary for treatment of the joint disease.

Flunixin Meglumine

Similar to phenylbutazone, flunixin meglumine (Banamine or Finadyne) is capable of suppressing PGE₂ production in inflammatory exudates. A typical dose used in the horse is 1.1 mg/kg. The drug can be administered orally, intramuscularly, or parenterally. Intramuscular injection should be avoided, if possible, because it has been associated with necrotizing clostridial infections. The action of flunixin meglumine administered orally or parenterally begins after 2 hours and can extend to 30 hours, with maximal effect in the first 16 hours. It is also presumed to accumulate in areas of inflammation.

Flunixin meglumine is used most commonly for treatment of visceral pain in the case of colic. However, its use is becoming slightly more common for treatment of some forms of joint disease. For the mild lamenesses, phenylbutazone is probably a better choice because it is less expensive. Traditional belief is that the use of flunixin meglumine is probably best saved for cases of soft tissue inflammation.

In these authors' opinion it can be useful in cases of severe synovitis, capsulitis, sprains, or septic arthritis.

The toxicity of flunixin meglumine is not as well described as that of phenylbutazone. No adverse clinical signs are present in horses administered three to five times the recommended dose for 5 to 10 days. However, the potential for toxicity still exists because this drug also inhibits COX-1 more than the COX-2 pathway. Therefore administration to debilitated, young or dehydrated horses should be avoided, if possible.

Ketoprofen

When first introduced, ketoprofen (Ketofen) was supposed to be superior to other NSAIDs because it was supposed to inhibit the cyclooxygenase and 5-lipoxygenase pathways. This obviously would broaden its antiinflammatory effects by blocking production of leukotriene-B₄ (LTB₄). However, *in vivo* studies have demonstrated that it blocks PGE₂ production similar to other NSAIDs, but it has no effect on LTB₄ production.

Clinically, ketoprofen is administered mostly to foals because it has the less propensity to cause gastrointestinal ulceration when compared with flunixin meglumine and phenylbutazone. The typical daily dose is 2.2 mg/kg administered once or twice a day parenterally. In an experimental model of synovitis in adults, ketoprofen suppressed PGE₂ levels, but it was not as good as phenylbutazone in decreasing lameness, synovial fluid effusion, and PGE₂ levels. Therefore it is used rarely in case of joint disease in adult horses but could be used with some success in cases of mild synovitis and capsulitis.

Meclofenamic Acid

Meclofenamic acid (Arquel) has a similar effect to phenylbutazone. The recommended daily dose of the oral granule is 2.2 mg/kg. It has a much slower onset of action (36 to 48 hours) than other NSAIDs and has similar toxicity to phenylbutazone. Clinically, this drug has been shown to be best for management of chronic musculoskeletal problems. In clinical trials, it improved 61% of horses with some form of osteoarthritis. In fact, when compared with phenylbutazone therapy for 7 days, it was shown to improve 60% of the horses with navicular syndrome or osteoarthritis, whereas phenylbutazone improved only 36%. However, because of its high cost, meclofenamic acid has been sparingly used in clinical situations.

Aspirin

Aspirin (acetylsalicylic acid) can irreversibly acetylate and inhibit cyclooxygenase. It also has been demonstrated to inhibit proteoglycan synthesis. The oral dose used in horses is 25 mg every 12 hours on day 1 of treatment, followed by 30 mg every 24 hours thereafter. Clinical use for joint disease is limited in the horse, however, because of its ability to inhibit platelet aggregation and thrombus formation, it could be used on suspected thromboembolic subchondral bone disorders that may affect the joint. Otherwise, it is probably best used for musculoskeletal conditions such as navicular syndrome and laminitis.

Naproxen

The analgesic effects of naproxen (Equiproxen) are similar to those of phenylbutazone, but it has a greater anti-inflammatory effect in experimental equine myositis. It originally was marketed for muscular conditions but has been used successfully in humans for joint disease. The recommended daily dose is 10 mg/kg orally, and it appears to have a wide margin of safety in horses. Clinical use of this NSAID for joint disease in horses is limited, but based on its use in humans, it has the potential for future benefits in the horse.

Carprofen

Carprofen (Rimadyl) is a relatively new NSAID for use in the horse. It is also capable of modestly reducing the concentration of PGE₂, but both phenylbutazone and flunixin meglumine are superior in this regard. It does not inhibit COX-2 activity in equine blood. However, experimentally, it reduces the volume of swelling that occurs as a result of inflammation in ponies. The suggested dose for the horse is 0.7 mg/kg administered orally or parenterally once daily. Another higher dose (4 mg/kg IV) has been shown to have a greater effect on the reduction of PGE₂ and a moderate effect on reduction of leukotriene-B₄ levels. However, the horse appears to tolerate the 0.7 mg/kg dose better. Intramuscular administration should be avoided because it has been demonstrated to increase CPK levels in horses. Clinical use of carprofen for joint disease in the horse is currently limited. It may prove to have a significant benefit because it has proved successful in experimental studies in dogs. In addition, it has been demonstrated to actually increase proteoglycan synthesis by equine chondrocytes and explants *in vitro*.

SODIUM HYALURONATE (HYALURONAN)

Hyaluronic acid is a linear polydisaccharide and polyionic nonsulfated glycosaminoglycan. It is an important component of both synovial fluid and articular cartilage. In synovial fluid, hyaluronan confers viscoelasticity, establishes boundary lubrication, influences synovial fluid composition through steric hindrance, and modulates the chemotactic response. In articular cartilage, hyaluronic acid provides the primary backbone to which proteoglycan aggregates attach. In the presence of joint disease, the hyaluronic acid concentration in synovial fluid generally is reduced.

The formulations of hyaluronic acid for intravenous injection (Legend) contain 40 mg (4 ml) of exogenous hyaluronic acid. How this intravenous hyaluronic acid achieves therapeutic levels in the joint is unknown. It is assumed that hyaluronic acid is localized to the highly vascularized synovial membrane. It is therefore possible that intravenous administration provides the synoviocytes with more hyaluronic acid than intraarticular injection. Horses used in a controlled osteochondral fragmentation model of equine osteoarthritis received three doses of Legend starting at day 13 postoperatively, followed by two weekly injections. The horses treated with intravenous hyaluronic acid had less lameness, less synovial mem-

brane inflammation and lower synovial fluid total protein and PGE₂ concentrations when compared to controls, 72 days after fragment induction.

Intravenous hyaluronic acid is used therapeutically and prophylactically. Therapeutically, it is important to choose the proper case to achieve success. Hyaluronic acid works best for those joint injuries with soft tissue inflammation. Although it is thought to not be successful for cases of established osteoarthritis, anecdotal evidence suggests that it may be beneficial in some instances of osteoarthritis. Intravenous hyaluronic acid works best for mild to moderate cases of synovitis, capsulitis, and strain injuries when combined with proper rest periods. The treatment regimen used by the author for this type of injury includes a series of three or four weekly injections followed by biweekly or monthly injections, depending on the use of the horse and economic constraints. Systemic hyaluronic acid also works well to decrease inflammation after arthroscopic removal of osteochondral fragments. This treatment regimen usually is started immediately postoperatively at the discretion of the surgeon. Again, three to four weekly doses are administered, and administration can be either discontinued or continued biweekly or monthly.

Prophylactic administration of intravenous hyaluronic acid is often done at biweekly or monthly intervals. A prospective blinded study of racing Quarter Horses prophylactically administered hyaluronic acid every 2 weeks has shown positive trends for improvement but did not diminish the amounts of other medication concurrently administered to these horses. Local intraarticular injection of hyaluronic acid combined with a corticosteroid may be more appropriate in these conditions. Lately some anecdotal evidence surfaced that a beneficial effect may be seen as soon as 48 hours after treatment, prompting some use of the medication before an event.

POLYSULFATED GLYCOSAMINOGLYCANS

Polysulfated glycosaminoglycans (PSGAGs) are a group of polysulfated polysaccharides deemed to be chondroprotective. Under new terminology, this drug would be referred to as a *disease-modifying osteoarthritis drug (DMOAD)*. Drugs with this classification should prevent, retard, or reverse the morphologic cartilaginous lesions of osteoarthritis and should have some capability to prevent cartilage destruction.

The precise mechanism of action of PSGAGs is unknown. The drug is a heparinoid that binds to cartilage and inhibits various enzymes and potentially some cytokines involved in cartilage degradation. In addition, it directly inhibits PGE₂ synthesis and stimulates synthesis of sodium hyaluronate and glycosaminoglycans. Osteoarthritic tissue appears to be more sensitive to the treatment effects of PSGAG than normal tissue.

Adequan

Historically, Adequan is the most commonly used PSGAG. Few studies show the efficacy of intramuscular administration of Adequan to horses. Absorption via intramuscular route has been documented sufficient to provide antiin-

flammatory effects within the joint when administered every 4 days. Intraarticular administration of Adequan has resulted in decreased development of osteoarthritis, but the same effect could not be demonstrated with intramuscular injections. However, anecdotally, this protection is also present when the drug is administered intramuscularly.

Clinically, Adequan commonly is used by practitioners involved with racehorses or show horses. According to a large survey of equine practitioners, Adequan was felt to be moderately effective for idiopathic and acute synovitis, subacute (mild radiographic changes) and chronic osteoarthritis (moderate to severe radiographic changes). In addition, when compared to hyaluronic acid, Adequan was more effective for subacute osteoarthritis and less effective for idiopathic and acute synovitis.

This fits the historical opinion about this DMOAD. It has been commonly believed that it should be used with cartilage damage rather than with acute synovitis. These authors recommend Adequan use in horses with radiographic signs of osteoarthritis, especially moderate to severe changes. No set course of administration of Adequan intramuscularly has been established. Practitioners must find what works best for their practices. However, the recommended course is seven intramuscular injections of 500 mg 4 days apart. Some practitioners prefer to space the injections weekly, and some prefer to do more than seven injections. After seven injections, the drug may be discontinued, or continued at weekly or monthly injections, depending on the case and economic constraints. In addition, it can be used in cases with evidence of significant articular cartilage loss as seen arthroscopically. Adequan can be administered intraarticularly (with 0.5 ml amikacin) at 2 weeks postoperatively, followed by 500 mg at weekly intervals for seven treatments, or whatever is deemed necessary by the surgeon. Similar to hyaluronic acid, Adequan also has been administered prophylactically, starting with a typical regimen, followed by weekly or monthly intervals. Adequan is used commonly in the equine industry with good perceived success. It is probably best used for cases with radiographic evidence of osteoarthritis, whereas hyaluronic acid is best used for cases

of synovitis. The treatment regimen depends on the preferences of each practitioner.

Pentosan Polysulfate

Pentosan polysulfate (PPS; Cartrophen) is another DMOAD. The traditional formulation of PPS is the sodium pentosan polysulfate. However, a new calcium derivative also has been developed that is supposed to be absorbed more effectively than the sodium pentosan polysulfate after oral administration, giving it a potential for wider use. Pentosan polysulfate does not provide any analgesia; instead, it must correct the pathobiologic imbalances present within the joint to provide symptomatic relief. This occurs by inhibition of enzymes and modification of the binding of cytokines that cause destruction of the articular cartilage matrix. In addition, PPS stimulates synthesis of hyaluronic acid and proteoglycans. In humans, this drug has been used extensively as an antithrombotic and antilipidemic agent.

Reports of clinical use of PPS for equine joint disease are lacking, but it is anecdotally thought to decrease synovial effusion and decrease lameness. This may suggest its use should be reserved for cases of synovitis, capsulitis, and mild osteoarthritis. In addition, this drug may actually decrease the rate of subchondral bone necrosis and sclerosis via its vascular effects. However, more studies must be performed to determine this hypothesis.

Supplemental Readings

- Grant BD: Rest, exercise, and physical therapy programs. In McIlwraith CW, Trotter GW (eds): *Joint Disease in the Horse*, pp 213-223, Philadelphia, WB Saunders, 1996.
- McIlwraith CW, Frisbie DD, Kawcak CE: Current treatments for traumatic synovitis, capsulitis, and osteoarthritis. *Proceedings of the 47th Annual Meeting of the American Association of Equine Practitioners*, pp 180-206, 2001.
- McIlwraith CW: General pathobiology of the joint and response to injury. In McIlwraith CW, Trotter GW (eds): *Joint Disease in the Horse*, pp 40-77, Philadelphia, WB Saunders, 1996.

CHAPTER 10.18

Extracorporeal Shock Wave Therapy

SCOTT McCCLURE

Ames, Iowa

MARKUS MAIER

Munich, Germany

CHRISTOPH SCHMITZ

Rostock, Germany

Extracorporeal shock wave lithotripsy is currently the standard therapy for humans with urolithiasis. Over the last decade, the use for extracorporeal shock wave therapy (ESWT) has been extended to treat gallstones, pancreatic stones, and salivary stones. In addition to the stone disintegrating effects, ESWT has been applied in orthopedics for more than 10 years. The biologic effects of ESWT are not restricted to the disintegration of mineral deposits. ESWT is also utilized for pain relief, stimulation of bone remodeling, and neovascularization of bone-tendon interfaces. For example, ESWT has been introduced into human and veterinary orthopedics for multiple applications including the treatment of delayed fracture healing and for tendon and ligament injuries.

Knowledge of the physical properties of shock waves is needed for understanding proper application, mechanisms of action of ESWT and for interpreting the results of research studies dealing with ESWT.

PHYSICAL PROPERTIES OF SHOCK WAVES AND SHOCK WAVE GENERATION

Shock waves are mechanical (i.e., acoustic) pressure pulses. At the wave front, pressure rises within nanoseconds from atmospheric pressure to the maximum positive pressure followed by an exponential decay to atmospheric pressure (Figure 10.18-1). Next, negative pressure follows the exponential decay, and finally pressure returns to atmospheric. The duration of a shock wave does not exceed 10 μ s. Peak positive pressure (P_+) can range between 5 megapascal (MPa) to more than 100 MPa (1000 times atmospheric pressure). Peak negative pressure (P_-) is between 10% and 50% of P_+ . Shock waves have a rapid rise time (T_r) from less than 1 ns to 500 ns and the entire pulse width (T_w) is between 200 ns and 500 ns. The duration of T_w is important with respect to the amount of energy delivered. The values P_+ , P_- , T_r , and T_w of a shock wave depend on the type of shock wave generator and the settings selected. For example, settings for P_+ may vary between 20 MPa and more than 120 MPa.

For clinical applications, it is necessary to focus the shock wave. To achieve this, different mechanisms are

available, depending on the physical type of shock wave generation (Figure 10.18-2). In electrohydraulic shock wave devices, shock waves are generated by a spark, comparable to the spark plug of a car. The spark discharge generates a plasma bubble in the converting medium. The plasma bubbles compress the surrounding fluid. The pressure waves generated by this compression spread out in a spherical manner and are focused by an elliptic reflector. In electromagnetic shock wave devices, shock waves are generated by a magnetic field induced by an electric current impulse in a coil. The magnetic field repels a membrane, which leads to compression of the converting medium. By compressing the converting medium, shock waves are generated and focused by an acoustic lens or by an elliptic surface as in the electrohydraulic devices. In piezoelectric shock wave devices, shock waves are generated by quartz crystals oscillating in an electric field. The spherical shape of the transducer usually focuses the waves.

With a focused shock wave a three-dimensional shock wave field occurs with a complex spatial and temporal distribution of positive and negative pressure. An important parameter of this shock wave field is the focal point, which usually is shaped like a cigar. An important interrelation exists between the degree of focusing of a shock wave device and the physical properties of the shock waves. For example, a shock wave source characterized by a tight focus produces a higher P_+ in a smaller area than a shock wave source characterized by a larger focal area. Thus the focal size determines both energy and energy flux density of the shock waves produced by the shock wave source.

Radial Pressure Wave Therapy

Ballistic or radial pressure wave generators are also available; however, they do not produce a true extracorporeal shock wave as defined by the industry. They use mechanical concussion to generate a pressure wave with a slower rise time and a negative component that is of the same order as the positive component. The kinetic energy of a projectile driven by compressed air is transmitted by an

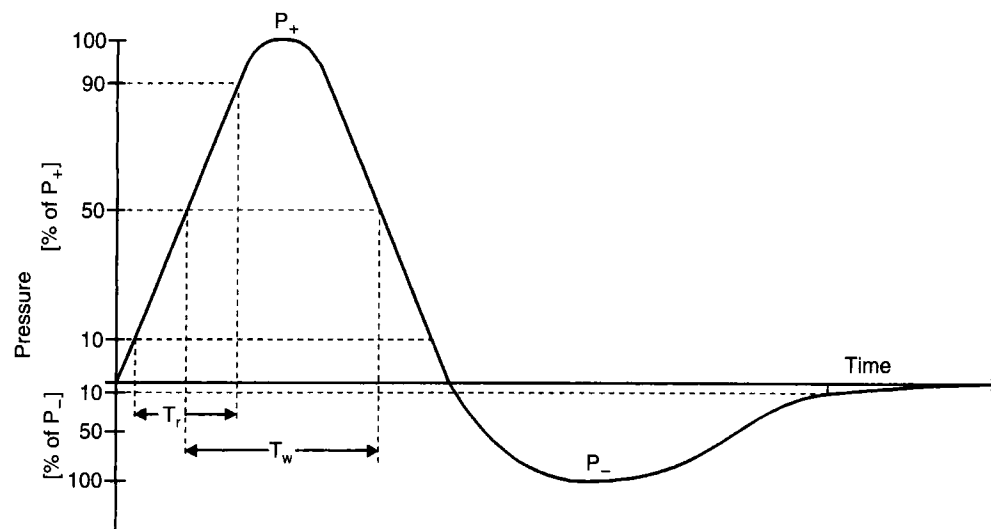


Figure 10.18-1 Graphic representation of a shock wave, with shock wave pressure as a function of time. P_+ , Peak positive pressure; P_- , peak negative pressure; T_r , rise time; T_w , pulse width.

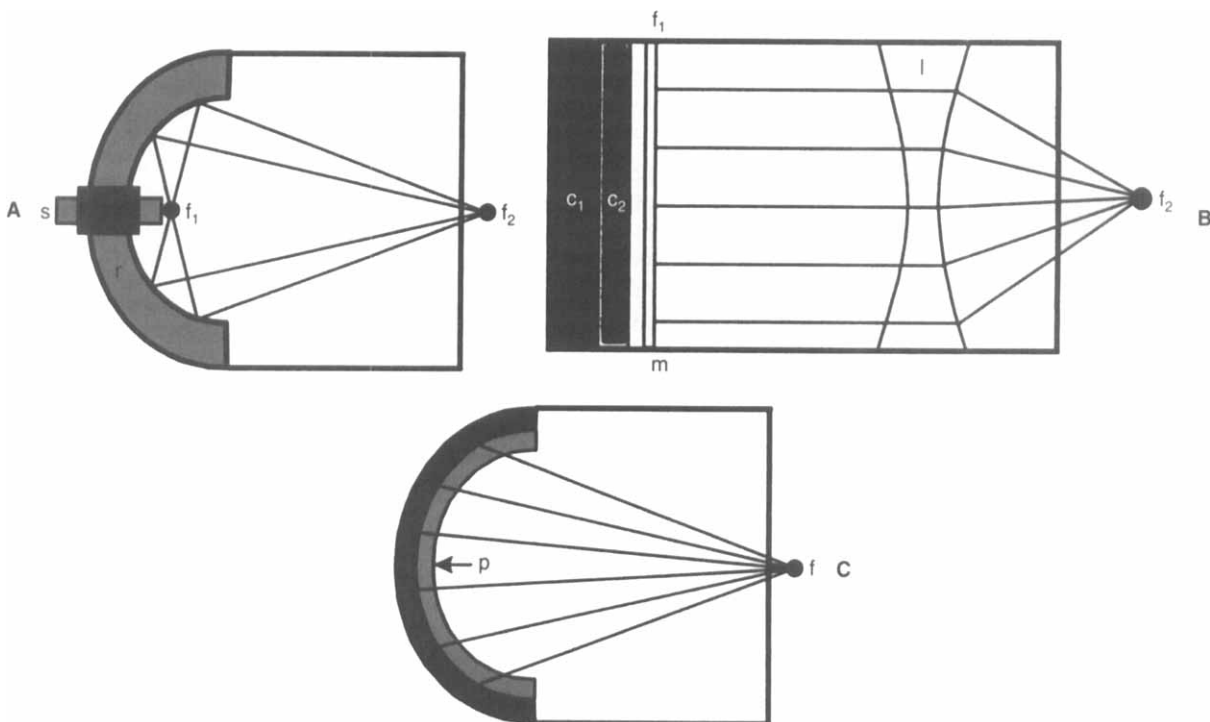


Figure 10.18-2 Schematic diagrams of three shock wave generators. **A**, An electrohydraulic shock wave generator has a spark gap (s) that initiates the pressure wave at the first focal point (f_1) and is focused at the second focal point (f_2) by the reflector (r). **B**, The electromagnetic generator uses a capacitor (c_1) and coil (c_2) to move the membrane (m) that starts the pressure wave that is focused by the lens (l). **C**, The piezoelectric shock wave generator has piezocrystals (p) arranged in a sphere that create the pressure wave.

elastic concussion to the probe. No focusing mechanism exists, and the pressure wave declines in an inverse square proportion to the distance from the source. Therefore the maximal energy is delivered to the skin surface rather than deeper tissues and is not discussed in this chapter.

Energy Flux Density within Shock Wave Fields

Shock wave energy is an important parameter for medical applications. As noted above, shock wave energy may be distributed over large or small areas. Shock wave devices concentrate acoustic energy into small focal areas to increase physiologic effects within the target area while minimizing the potential undesired side effects in surrounding tissue. The concentrated shock wave energy per unit area is an important parameter. The term *energy flux density (EFD)* is used to describe the shock wave energy flowing through an area oriented perpendicular to the direction of propagation. The EFD is defined as the amount of shock wave energy within 1 square millimeter of the focal area of the acoustic field. The energy flux density is given either as the positive energy flux density (ED_+) or as the total energy flux density (ED). The energy flux density is measured in millijoule per square millimeter (mJ/mm^2), and this value can be used to make comparisons between treatment protocols.

EFFECTS OF SHOCK WAVES IN TISSUE

Shock waves exhibit both direct and indirect effects. The direct effects of shock waves are mediated at border zones between two tissues with different acoustic impedances. The acoustic impedance is defined as the product of its density and the speed of sound within the medium (Ns/m^3). Acoustic impedances of various materials and tissues are given in Table 10.18-1.

Shock waves are deflected at the border zones of tissues with different acoustic impedances including reflection and refraction of the wave. This results in release of kinetic energy at the junctions, which can cause tissue alterations. For example, a kidney stone can be cracked by a certain

amount of shock wave energy, whereas in bone, the same amount of shock wave energy does not result in fragmentation. The release of kinetic energy at interfaces of different acoustic impedances is crucial in planning ESWT. Shock waves must never be focused on gas-filled cavities such as lung or intestine. The acoustic impedance of air is markedly lower than the acoustic impedance of soft-tissue such as muscle. Thus virtually all acoustic energy is reflected at the border zone. At such an interface the phase of the pressure is reversed, turning P_+ into rarefaction pressure and vice versa. As a consequence, maximum pressure at the border zone may turn into rarefaction pressure up to twice the extent of the former P_+ and may result in considerable tissue damage at the border zone.

The indirect effects of shock waves are mediated by cavitation. Cavitation is defined as the appearance of bubbles in a fluid. At the beginning of the phase of negative pressure of a shock wave, water molecules separate and vacuum bubbles form. Vapor from the surrounding fluid is collected within the bubbles, causing them to expand during the course of negative pressure phase to more than tenfold of the original bubble volume. At the end of the phase of negative pressure, a return to atmospheric pressure causes the bubbles to collapse with a speed of 1 to 9 meters per second, comparable with an implosion (Figure 10.18-3). In addition to pressure pulses that are a result of the implosion, water jets with highly destructive effects may arise.

Much interest exists in how these direct and indirect effects of shock waves affect tissue. Although much information is available concerning how shock waves fracture uroliths, the mechanisms of shock wave cellular stimulation are just beginning to be investigated.

Table 10.18-1
Acoustic Impedance of Important Materials and Tissues

Material/ Tissue	Acoustic Impedance [$\times 10^3 \text{ Ns}/\text{m}^3$]
Air	429
Lung	260-460
Fat	1380
Water	1480
Kidney	1630
Liver	1650
Muscle	1650-1740
Bone	3200-7400
Urolith	5600-14,400

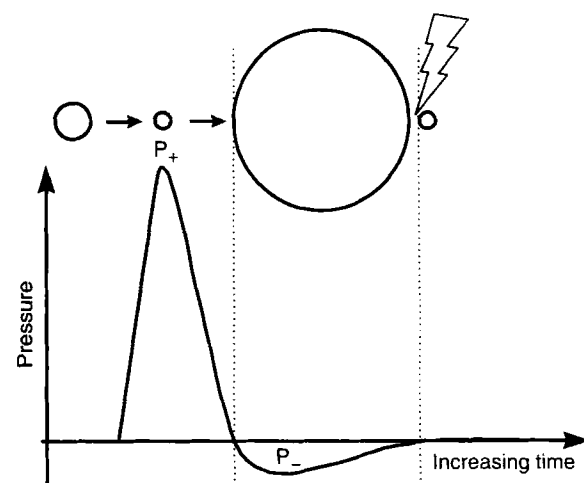


Figure 10.18-3 Schematic description of the cavitation effect. Small, gas-filled bubbles are compressed by the first part of a shock wave (i.e., the part of the shock wave with positive pressure). During the second part of the shock wave (i.e., the part of the shock wave with negative pressure) the compressed bubbles enlarge. At the end of the second part of the shock wave, atmospheric pressure is reached and bubbles implode with high velocity. From this implosion, small high-speed water jets arise with a highly destructive effect. P_+ , Peak positive pressure; P_- , peak negative pressure.

Biologic Effects of Extracorporeal Shock Wave Therapy

In vitro, specific alterations of the shock wave characteristics can affect how tissues are affected. Both variation of T_r and the ED influences the effects on cells, ranging from induction of stress fibers and intercellular gaps to complete detachment of endothelial cells and damage to the basement membrane. Studies that look at dose effects of shock waves consistently indicate a minimum energy level that must be attained to stimulate cells and a level, which when exceeded, leads to cellular damage. Shock wave stimulation of the production of TGF- β by bone marrow stromal cell cultures was found to be dose related with no effect at lower energy doses rising to a maximal effect then dropping off to a deleterious effect with a higher dose. When human cancellous bone cells in culture are treated with shock waves, a short-term effect of cellular death exists but a medium term effect of cell-stimulation, which was dependent upon the number of pulses delivered. Shock waves also have been proven to be an effective mechanism for transfection of oligonucleotides in cells and to transfer chemotherapeutics into neoplastic cells.

One of the first studies on the effect of shock waves on fracture healing was completed in rats. Middiaphyseal humeral fractures were created and the fractures were treated with ESWT on days 2, 5, 9, 14, and 19 postfracture. Treated bones were found to be heavier than controls, had breaking strength 30% greater than controls, and healed faster. In another fracture healing study in dogs, bilateral tibial osteotomies were stabilized with a 6-hole plate to maintain a 3-mm gap at the osteotomy site. Shock wave-treated legs had significantly more callus formation at 12 weeks than the untreated legs. Histologically, treated limbs had more cortical bone than controls. In yet another study, hypertrophic nonunions were created in 10 Beagles by a distal radial osteotomy. At 12 weeks, five dogs were treated with shock waves and five served as controls. Four of five treated dogs had osseous union 12 weeks after treatment and one of five control dogs progressed to an osseous union.

In two soft tissue studies, dose-related effects of shock waves were identified. Low-dose ESWT enhanced the reepithelialization of skin wounds in pigs in both normal tissue and in tissue in which healing had been delayed by radiation. High-dose ESWT inhibited reepithelialization. ESWT has been shown to stimulate neovascularization of the Achilles tendon-bone interface in dogs. When dose-related effects were evaluated on the rabbit, Achilles EFD exceeding 0.28 mJ/mm² induced necrosis.

In all cases, the biologic effects of shock waves depended on the number of shock wave pulses and the ED administered. The evaluation of studies involving ESWT must consider these points.

Analgesic Effect

A posttreatment analgesic effect has been reported following ESWT. In humans, the analgesic effects have been noted, but no studies that identify the mechanism or duration have been completed. Several hypotheses exist regarding to the mechanism, including destruction of nerves, nerve receptors, and central control of sensory in-

put (gate control theory). None of these hypotheses truly are supported by research. ESWT is known to raise the threshold potential of neural membranes. The possibility exists that after therapy a horse may be at risk of incurring a significant injury if worked without full sensory input.

EQUINE APPLICATIONS OF SHOCK WAVE THERAPY

Shock wave therapy has been used for equine musculoskeletal diseases for the last 3 to 4 years. At this time the indications for use are still being developed and little controlled data are available. The indications for ESWT in the horse are similar to human therapies, insertional desmopathies, and for stimulation of bone remodeling.

Suspensory Desmitis

Multiple users of ESWT have indicated that suspensory desmitis responds well to treatment. Initial clinical observations indicate that the lesions heal faster when ESWT is administered at 2- to 3-week intervals during the healing process. EFDs should be lower (0.1 to 0.2 mJ/mm²) during the acute phases and are increased (0.5 to 0.8 mJ/mm²) in the more chronic cases. Necrosis of the ligament may be induced by excessive energy levels. Initial data from two different clinics indicate that 7/8 and 5/6 horses showed clinical improvement, which persisted at follow-up examinations 3 months and 6 months posttreatment, respectively. These numbers have increased notably since these reports with similar responses. Controlled studies are under way.

Digital Flexor Tendonitis

The experience of multiple users indicates that superficial and deep digital flexor tendonitis appears to respond to ESWT by decreasing the cross sectional area of the lesion faster than traditional conservative methods. As with suspensory desmitis, a series of treatments with comparable energy levels are being used.

Osteoarthritis of the Distal Intertarsal and Tarsometatarsal Joints

The first published study of ESWT in the United States was a case series of horses with bone spavin. At follow-up examination 90 days after treatment, 80% (59/74) horses had improved at least 1 lameness grade. These horses were treated under general anesthesia at high energy (0.89 mJ/mm²). The shock waves were focused with the aid of fluoroscopy in the joint spaces at the site of the pathology. The expectation that lameness resolution was the result of stimulated ankylosis was not supported radiographically. The mechanism of resolution is unknown but potentially subchondral bone remodeling, changes in intramedullary pressure and analgesic effects of shock waves are potential mechanisms.

Dorsal Periostitis

Bucked shins are the result of the bone remodeling in response to loading. Bone remodeling in the cannon bone

clearly is stimulated by ESWT with osteogenesis present from the periosteal to endosteal surfaces. Initial clinical evaluation of the use of ESWT for treating dorsal periosteal reactions is encouraging. Horses that develop pain and periosteal remodeling have been maintained in training by utilizing ESWT at 1- to 2-week intervals for three treatments.

Stress Fractures

As experimental data support the stimulation of non-union fracture healing by ESWT, the application of ESWT to stress fractures in horses seems to be a logical approach. At this time, only clinical impressions exist that stress fractures heal faster after treatment. These authors' data would support this. One of the major concerns in dealing with stress fractures in racehorses is the decision on when it is safe to return the horse to work. The reported analgesic effect of ESWT may lead to horses being worked before the bone is adequately healed. Repeated nuclear scintigraphy and radiography may be helpful in determination of when the bone is healed adequately.

Navicular Syndrome

In a group of 16 horses with navicular syndrome, which were treated with ESWT, it was found that 70% of the treated limbs improved at least one grade of lameness. Treatment consisted of a single session at high energy (0.9 mJ/mm²) with 1000 pulses applied through the frog and 1000 pulses applied between the heel bulbs. Before treatment, the frog is pared and the foot trimmed to allow good coupling. The foot is then soaked in water for 12 hours before treatment to hydrate the frog to facilitate shock wave transmission. Horses with erosions of the flexor cortex and those with navicular suspensory ligament enthesopathy have responded less favorably. It would seem that the enthesopathy should respond to treatment. Failures may be due to the difficulty in obtaining a window to focus the shock waves in this area. Horses that respond appear to remain improved for at least 1 year after treatment; however, recurrence at some point would be expected.

Multiple claims have been made relative to other musculoskeletal diseases; however, fewer cases are in these groups, making objective assessment difficult. It is unlikely that ESWT is helpful in all musculoskeletal problems.

POTENTIAL COMPLICATIONS

In humans and small animals, petechiation of the skin at the treatment site has been reported. This is not com-

monly seen in the horse. Excessive energy and or pulse numbers may lead to tissue necrosis. It is therefore important to keep in mind that more is not necessarily better. Gas/tissue interfaces should be avoided as previously noted because of the potential damage to lung and intestine. Intimal damage in arteries may be seen after ESWT, so major blood vessels should not be in the focal zone. The effects on nerve tissue have not been identified fully, so important nerves also should be avoided. Active physes should be avoided because studies have demonstrated premature closure of the physis in laboratory animals after ESWT.

Supplemental Readings

- Chow GK, Streem SB: Extracorporeal lithotripsy. Update on technology. *Urol Clin North Am* 2000; 27:315-322.
- Delius M, Draenert K, Al Diek Y et al: Biological effects of shock waves: in vivo effect of high energy pulses on rabbit bone. *Ultrasound Med Biol* 1995; 21:1219-1225.
- Delius M, Enders G, Heine G et al: Biological effects of shock waves: lung hemorrhage by shock waves in dogs—pressure dependence. *Ultrasound Med Biol* 1987; 13:61-67.
- Folberth W, Kohler G, Rohwedder A et al: Pressure distribution and energy flow in the focal region of two different electromagnetic shock wave sources. *J Stone Dis* 1992; 4:1-7.
- Howard D, Sturtevant B: In vitro study of the mechanical effects of shock-wave lithotripsy. *Ultrasound Med Biol* 1997; 23:1107-1122.
- McCarroll GD, McClure SR: Extracorporeal shock wave therapy for treatment of osteoarthritis of the tarsometatarsal and distal intertarsal joints of the horse. *Proceedings of the 46th Annual Meeting of the American Association of Equine Practitioners*, pp 200-202, 2000.
- McClure SR, Vansickle D, White MR: Extracorporeal shock wave therapy: what is it? what does it do to equine bone? *Proceedings of the 46th Annual Meeting of the American Association of Equine Practitioners*, pp 197-199, 2000.
- Rompe JD, Kirkpatrick CJ, Kullmer K et al: Dose-related effects of shock waves on rabbit tendon Achilles: a sonographic and histological study. *J Bone Joint Surg Br* 1998; 80:546-552.
- Scheuch B, Whitcomb MB, Galuppo L et al: Clinical evaluation of high-energy extracorporeal shock waves on equine orthopedic injuries. *Proceedings of the 19th Annual Meeting of the Association of Equine Sports Medicine*, pp 18-20, 2000.
- Steinbach P, Hofstaedter F, Nicolai H et al: Determination of the energy-dependent extent of vascular damage caused by high-energy shock waves in an umbilical cord model. *Urol Res* 1993; 21:279-282.
- Valchanou VD, Michailov P: High-energy shock waves in the treatment of delayed and nonunion of fractures. *Int Orthop* 1991; 15:181-184.

CHAPTER 10.19

Complementary Therapies for the Treatment of Musculoskeletal Disorders

KEVIN K. HAUSSLER

Ithaca, New York

The most common prescriptions for the conservative management of chronic musculoskeletal injuries in horses include pain management with drugs such as phenylbutazone and limited activity; for example, stall rest or paddock turnout. In humans, the chiropractic, acupuncture, and physical therapy professions use additional adjunctive diagnostic and therapeutic modalities proven effective for the management of select musculoskeletal disorders. Many of these same diagnostic and treatment regimes may be directly applicable to equine patients.

Unfortunately, currently limited objective measurement or rehabilitation tools exist to specifically assess soft tissue or articular pain, reduced flexibility and joint stiffness, muscle hypertonicity, alterations in proprioception, or loss of strength associated with long-term musculoskeletal or nerve dysfunction. The diagnostic evaluation of the majority of musculoskeletal disorders involves advanced imaging techniques geared toward identification of structural pathology that rely less on functional assessment. The downfall of relying solely on a structural diagnosis is the frequent poor correlation between structural pathology, such as early osteoarthritis, and clinical signs of dysfunction, including vague pain or stiffness. For minor but clinically significant perturbations of the musculoskeletal system, a detailed and more critical functional assessment is required. A multidisciplinary approach that includes medical, surgical, chiropractic, acupuncture, and physical therapy often proves to be the most effective means for the diagnosis and management of chronic or challenging musculoskeletal disorders in equine athletes.

As with any aspect of veterinary medicine, a thorough physical examination and diagnostic evaluation is important to establish as definitive a diagnosis as possible to assist in the development of specific treatment and rehabilitation protocols. Unfortunately, if a musculoskeletal problem is localized to the axial skeleton, it is often difficult to establish a definitive diagnosis because of the current limitations of physical assessment or diagnostic imaging. In these instances chiropractic, acupuncture, and physical therapy may provide a more in-depth or specialized examination of the problem area and provide an additional option for conservative management. Therapeutic trials often are offered to clients because limited clinical research is currently available to scientifically substantiate

the use of many forms of complementary and alternative therapies in horses.

MANUAL THERAPY

The human professions involved in providing various forms of manual therapy include chiropractic, osteopathic, physical therapy, and massage. They have evolved to provide effective nonmedical and nonsurgical approaches for the management of specific musculoskeletal issues. Many of these techniques have direct clinical application to equine athletes. Chiropractic should be considered a form of complementary therapy because it is indicated primarily for musculoskeletal conditions and is rarely indicated for other nonmusculoskeletal conditions.

The field of equine manual therapy is in its infancy and recommendations for treatment are often based on exclusion of overt musculoskeletal pathology that may provide potential contraindications and on the lack of a definitive diagnosis based on current orthopedic, neurologic, and imaging procedures. Nonspecific musculoskeletal disorders of the axial skeleton and the proximal limbs are the primary areas of focus for chiropractors. Rehabilitation of distal limbs injuries causing stiffness or pain resulting from mechanical restrictions that have been medically or surgically managed is also a potential indication for manual therapy.

The majority of manual therapy cases, by definition, involve generalized joint stiffness, muscle soreness, vague soft tissue or articular pain, and nonspecific lameness (Box 10.19-1). Patients often have extensive orthopedic, neurologic, diagnostic imaging, and medical evaluations without a specific diagnosis. The primary indication for manual therapy is joint stiffness related to acute or chronic articular immobilization or dysfunction, soft tissue or osseous restrictions, poor performance, or an altered gait not associated with overt lameness. Chronic lower limb pathology often induces compensatory changes in the upper limbs or axial skeleton, for example, chronic laminitis induced changes in upper limb muscle development or flexibility. Manual therapy techniques are indicated to assess and treat the secondary and sometimes more clinically significant musculoskeletal compensations. Musculoskeletal conditions that are chronic or recurring, not

BOX 10.19-1**Potential Clinical Indications for Complementary Therapy Evaluation or Treatment**

Poor performance
 Back, wither, or neck pain
 Reduced neck or back flexibility
 Inability to raise or lower the head and neck
 Localized or generalized muscle hypertonicity
 Vague lameness
 Uneven or asymmetric gait
 Recent change in spinal conformation
 Difficult or improper saddle fit
 Discomfort with saddle placement
 Resentment at tightening of the cinch or girth
 Stiffness and slow in warming up
 Bucking or pinning of the ears when ridden
 Lameness only when ridden
 Constant reliance on one rein or line
 Difficulty with a lead or gait transition
 Refusal to jump
 Resistance to collection
 Poor hindlimb impulsion
 Poor coupling at the lumbosacral junction
 Difficulty with turning in one direction
 Consistent stumbling or dragging of a toe
 Muscle mass asymmetry
 Osseous pelvic asymmetry
 Inability or unwillingness to stand squarely on all four limbs
 Difficulty standing for the farrier
 Holding of the tail to one side
 Resentment at being groomed
 Behavior or avoidance problem

readily diagnosed, or do not respond to conventional veterinary care also may be indications for chiropractic consultation.

Manual therapy techniques have great diagnostic value when used for a detailed and direct evaluation of axial skeleton function, which unfortunately is not routinely available in veterinary medicine. The diagnostic value of chiropractic evaluation is especially evident during pre-purchase examinations, at "vet checks" during athletic competitions, for monitoring the effectiveness of musculoskeletal rehabilitation protocols, assessment of the contribution of poor saddle fit to back pain, and determination of the clinical significance of documented axial skeleton pathology in the absence of obvious clinical signs such as ataxia or lameness.

Diagnostically, the individual vertebrae of the axial skeleton are actively and passively evaluated for restricted motion, pain or muscle guarding during flexion-extension, left and right lateral bending, and rotation movements. If altered function is localized to a specific region, for example, a primary back or neck problem, then addi-

tional diagnostic or imaging modalities may be indicated, based on the clinical history and perceived severity of the lesion. If the problem is more regional or generalized, then the musculoskeletal dysfunction may be more compensatory in nature; secondary to a primary lower limb lameness such as hock osteoarthritis or neurologic disease such as equine protozoal myelitis. In these cases, concurrent medical and chiropractic care are indicated. Additional musculoskeletal conditions that benefit from manual therapy techniques include posttraumatic injuries, postsurgical complications, rehabilitation of joint stiffness, and the management of localized regions of muscle hypertonicity.

Manual therapy techniques often are used to evaluate objectively spinal mobility and upper limb flexibility, a musculoskeletal function rarely evaluated or directly treated in traditional veterinary medicine. The diagnostic challenge is to localize definitively the perceived stiffness to either intraarticular structures or periarticular soft tissues. Passively moving the individual limb articulations through full ranges of joint motion identifies affected articulations and the clinical significance of the joint stiffness. Restricted axial skeleton mobility can be assessed further and treated with "carrot stretches," which induce active joint range of motion. With a treat, the horse is enticed to bring its nose to the elbow region to evaluate neck stiffness and then along its rib cage to the point of the hip to evaluate back stiffness. Neck flexion also can be assessed with a treat positioned at the manubrium to evaluate poll flexion and at the front feet to evaluate lower cervical flexion. Assessment of individual vertebral segment motion restrictions can be identified and treated using specific equine manual therapy techniques, many of which have been modified from human techniques. The benefits of manual therapy include restoration of restricted joint motion associated with poor performance and reduced flexibility noted during specific athletic demands; for example, the horse bends well to the left but not the right.

Other indications of manual therapies for equine musculoskeletal injuries include acute or chronic pain and alterations in muscle tonicity. Algometry, which is a pain pressure threshold measurement, uses a hand-held calibrated instrument that records the amount of applied pressure per centimeters squared.

To objectively document the presence and severity of muscle or bone pain, recorded values are compared with predetermined standardized values in normal horses. In general, pressure measurements below 10 lb/cm² indicate the presence of pain and values above 20 to 30 lb/cm² indicate normal musculoskeletal sensation. This author's experience is that chiropractic care can effectively reduce musculoskeletal pain and increase joint mobility. However, reducing muscle hypertonicity with chiropractic techniques does not appear to always be reliable or consistent. Therefore concurrent use of acupuncture, stretching exercises, physical therapy or massage therapy often is indicated to assist in the reduction of local or regional muscle hypertonicity. A thorough diagnostic evaluation is required to identify soft tissue and osseous pathology, neurologic disorders, or other lameness conditions that may not be responsive to chiropractic care. Chiropractic is not a "cure all" for all neck or back problems and is not suggested for treatment of fractures, infections, neoplasia,

metabolic disorders, or nonmechanically related joint disorders. Serious diseases requiring immediate medical or surgical care must be treated by conventional veterinary medicine before any form of manual therapy is initiated.

ACUPUNCTURE

The human acupuncture profession has developed substantially in the United States in the last 30 to 40 years. Some controversy exists over the direct transfer of human acupuncture points to horses resulting from differences in the number of vertebrae and distal limb anatomy and the lack of formal clinical research to support or refute the use of acupuncture for specific equine disorders. Acupuncture can be considered a form of alternative therapy because it may be indicated for both musculoskeletal and nonmusculoskeletal conditions. The primary indications of acupuncture for equine musculoskeletal injuries include acute or chronic pain, trauma to various soft tissue, ligamentous or osseous structures, osteoarthritis, laminitis, muscle hypertonicity, and certain peripheral neuropathies.

Acupuncture does not have any known direct effects on reducing joint stiffness as do manual therapies. Therefore synergistic effects often are obtained with combined chiropractic and acupuncture treatment that cannot be obtained consistently with either modality by itself. Because acupuncture is a drug-free option for pain relief, its use or misuse has important implications in the performance or racing industries. Common methods of equine acupuncture include point stimulation acupressure, dry needling, aquapuncture with vitamin B₁₂, electroacupuncture, and laser puncture.

The primary benefit of acupuncture for musculoskeletal disorders is pain management via opioid (i.e., enkephalin and β -endorphin) and nonopioid pathways. Pain relief is often immediate but may have variable durations of effectiveness, depending on the type and severity of musculoskeletal dysfunction. Acute injuries often respond rapidly and require fewer treatment sessions, whereas chronic musculoskeletal conditions may require periodic or long-term treatment. Acupuncture is often the treatment of choice for trigger points, which are characterized by localized tight, painful bands of muscle at characteristic locations within large muscle groups. In humans, trigger points often are associated with tension headaches and chronic fatigue syndrome or fibromyalgia. Similar generalized myofascial pain syndromes are common in performance horses. Acupuncture, combined with manual therapy techniques such as massage, and stretching and with dietary modification such as a high fat diet, often are the only effective means for long-term management of chronic muscle pain and hypertonicity. Acupuncture, combined with the appropriate medical or surgical treatment, is an effective adjunct for the management of articular pain, bucked shins, splints, tendinitis, laminitis, or navicular disease. The immediate prurice use of acupuncture is banned by many racing jurisdictions and athletic organization regulations because of its potential misuse or analgesic properties. Further clinical research is indicated to assess the effectiveness of acupuncture for the multitude of pain-related musculoskeletal conditions encountered in equine practice.

PHYSICAL THERAPY

Veterinary professionals often recognize that "physical therapy" may be a vital component to address or help manage specific musculoskeletal conditions but rarely are they individually qualified to provide these services because of a lack of formal training in veterinary education. In addition, veterinary personnel rarely consult professionals in human physical therapy that do have specialized training in these specific modalities. Many physical therapists who work with humans are interested in collaborative work with veterinarians and eager to apply the various physiotherapy modalities to animal patients. Certain veterinary practice acts allow collaborative efforts by professionals trained in performing therapy with humans to work under the direct supervision of veterinarians on animal patients. Physical therapy modalities that may have direct application to musculoskeletal injuries in horses include devices that apply electrical currents for pain control or neuromuscular rehabilitation; thermal modalities such as heat or cold applications for influencing inflammatory mediator release and collagen extensibility; and mechanical approaches such as vibration, stretching, and training exercises for maximizing musculoskeletal rehabilitation.

The primary indications of physical therapy for equine musculoskeletal injuries include localized or generalized pain, joint motion restrictions, and altered muscle tonicity. Pain modulation can be provided by influencing inflammatory mediators, altering pain perception and transmission, and increasing β -endorphin levels. Physical therapy modalities involved in pain control include electrical stimulation, for example, muscle stimulation; transcutaneous electrical nerve stimulation (TENS); and the application of hot or cold, mechanical vibration, and electromagnetic modalities. Soft tissue and articular motion restrictions (i.e., stiffness) can be addressed directly with specific stretching exercises to induce creep and stress relaxation within fibrotic or shortened periarticular soft tissues. With minimal training, horses and their owners can be taught how to do simple but effective passive joint mobilization and active stretching exercises such as carrot stretches to improve both axial skeleton and limb flexibility. The application of heat or electrical stimulation can provide increased soft tissue extensibility, reduced inflammation and adhesion formation, and pain control to help facilitate the restoration of normal joint motion.

Abnormal muscle tone can be addressed with modalities that increase or decrease muscle contractility or coactivation and nerve conduction or inhibition. Some of these modalities include hydrotherapy, electrical stimulation, and rehabilitative exercises that specifically address issues of reduced flexibility, coordination, strength, and endurance. In humans, antiinflammatories and other drugs can be delivered into superficial soft tissues or articular structures via electrical currents (i.e., iontophoresis) or via mechanical sound waves (i.e., phonophoresis). Preliminary equine research indicates that a heavy hair coat, thick skin, and deep articular structures may limit the overall effectiveness of these novel drug delivery systems.

ANCILLARY MODALITIES

Nutraceuticals such as chondroitin sulfate and glucosamine are often indicated in osteoarthritis to assist in preserving or restoring cartilage health (see Chapter 1.8: “Nutraceuticals”). However, controversy exists on the oral absorption and bioavailability of some of these products in horses. Other products such as methylsulfonylmethane (MSM) provide a source of sulfur and are thought to have a role in maintaining the integrity and elasticity of connective tissue and the production of glycosaminoglycans. Herbal products such as devil’s claw have potential anti-inflammatory effects and have been recommended as an herbal supplement for horses that need to be on low levels of phenylbutazone for long periods of time. Arnica montana is a flower preparation applied topically for acute muscle trauma for its antiinflammatory and analgesic effects. Cayenne contains the active ingredient capsaicin, which can be applied topically to desensitize superficial sensory nerve endings to pain stimulation via depletion of substance P. The direct application of human nutraceuticals or herbal preparations to horses is often difficult because absorption, bioavailability, dosages, mechanisms of action, and side effects may vary between humans and horses.

Proper saddle fit and placement are important to help minimize back problems. The use of extraneous saddle pads or wedges is often a sign of potential saddle fit problems. Good saddle fit, like good shoe fit, should be individualized and not dependent on the type or amount of padding used. Biting problems can be common and veterinarians often have little formal training or clinical experience in evaluation or recommendation of changes in the type or severity of bit used. Apparent resistance to the bit or being heavy on the bit can originate from painful musculoskeletal sites distant to the mouth. The veterinarian’s task is to rule out lameness or pain in other locations, for example, a forelimb lameness or neck stiffness, which may contribute to the biting problem. Additional tack that needs to be evaluated is the appropriate use and fit of the noseband or cavesson, standing or running martingales, draw reins, and the chambon during lunging exercises. Evaluation of proper tack fit and use requires that the horse and rider are evaluated while participating in their specific equestrian activities. Horses should be relaxed and comfortable with any manipulation of the reins, bit, or saddle. Improper harness fit and the use of extraneous restraint devices are important issues for the Standardbred racehorse that need to be assessed as potential contributors to musculoskeletal dysfunction.

Improper or excessive training techniques may be noted while observing horses being lunged or worked over ground poles or cavalletti. Certain musculoskeletal disorders can be managed appropriately with minor alterations in the training or exercise programs. Rider evaluation by qualified instructors may help to correct rider imbalances that contribute to back problems or poor performance. Centered riding techniques developed by Sally Swift are good tools to become aware of important horse-rider interactions that may influence neck, back, or limb pain in equine athletes. In humans, Alexander and Feldenkrais practitioners seek to improve musculoskeletal efficiency and function through the use of nonhabitual movements

that stimulate balance, coordination, and body awareness. Similar equine TTEAM or TTouch techniques have been developed by Linda Tellington-Jones to assist in the management of certain chronic musculoskeletal injuries or pain behaviors. Utilizing equine socialization and herd instinct skills, training techniques developed by Monty Roberts, Tom Dorrance, John Lyons, Pat Parelli, and others are often effective for the management of behavioral or training issues associated with musculoskeletal pain or dysfunction.

INDICATIONS FOR COMPLEMENTARY THERAPY REFERRAL

The Integrative Medicine Service at the Cornell University Hospital for Animals (CUHA) is a unique specialty service with the sole responsibility of providing consultations, diagnostic evaluations, and treatment in chiropractic, acupuncture, and physical therapy modalities. A retrospective analysis of 50 randomly selected equine cases investigated the primary presenting complaints and clinical indications for complementary medicine referral to a university institution. The significant history and primary presenting complaint was related directly to the musculoskeletal system in 35 (70%) horses, with a specific complaint of neck problems in nine horses, back-related problems in 12 horses, forelimb lameness in 10 horses, and pelvic or hind limb lameness in 22 horses. Several patients presented with multilimb lameness or both back problems and concurrent lameness or neck problems. The other 15 (30%) of horses presented with performance-related problems (seven horses), behavior-related issues (three horses), and other nonspecific or nonmusculoskeletal problems (five horses).

The primary presenting complaints localized to the neck region included neck stiffness, altered neck curvature, upper cervical vertebral fractures, concurrent neck stiffness and forelimb lameness, stenotic cervical myelopathy, cervical facet osteoarthritis, and abnormal vaccine reactions (soft tissue swelling and neck stiffness). Concurrent chiropractic care was provided to reduce neck stiffness, pain, and muscle hypertonicity. Neurologic conditions such as stenotic cervical myelopathy and severe osteoarthritis are often contraindications for chiropractic care because of the risk of aggravating spinal cord compression or articular inflammation. In these situations, less aggressive modalities for restoring cervical mobility (for example, active stretches and chondroprotectants) were prescribed. Chiropractic evaluation provided a functional clinical evaluation of joint stiffness for identification of the vertebral level or laterality of the lesions.

The primary presenting complaints localized to the back included impinged spinous processes, undefined back soreness, poor performance, bucking while lunged or ridden, back stiffness, generalized longissimus muscle hypertonicity, renal disease, and episodes of recurrent colic. Concurrent chiropractic care was provided to reduce back pain and paraspinal muscle hypertonicity, or improve vertebral segment mobility. Additional complementary therapies that were recommended or applied included stretching exercises, acupuncture, alterations in training or exercise, changes in saddle fit, and massage therapy. Sad-

dle fit and saddle pad assessment always is indicated on initial visits for new clients and for pain localized to the caudal withers region. Attempts at identifying or treating withers pain or local muscle hypertonicity are often futile without knowledge of proper saddle fit or other tack usage. The pain and reduced performance associated with impinged spinous processes often are aggravated by extension movements because of the induced impingement of the affected spinous processes. "Belly lift" exercises that induce elevation of the withers and separation of the affected spinous processes greatly help in the conservative management of impinged spinous processes. Concurrent acupuncture or interspinous injections of local anesthetics and corticosteroids also may be indicated in the acute pain stages to help break the pain cycle. Extensive medical or surgical evaluations are indicated for renal disease or recurrent colic; however, chiropractic techniques can help to differentiate primary versus secondary musculoskeletal pain or dysfunction in difficult cases.

Lameness in the affected horses was related to single or multiple limb lameness, osteoarthritis, lower motor neuron (LMN) weakness associated with residual botulism toxicity, pelvic fractures, or stringhalt. Additional clinical signs included ataxia, osseous pelvic asymmetry, resentment to backing up, stifle lameness while going down hills only, and kicking out on the hind limbs. Several patients presented with a combined lameness and neck or back problems. Chiropractic provided valuable insights into the interaction and potential contribution of the lower limb lameness to the upper limb or back dysfunction, and vice versa. Concurrent medical, surgical, and chiropractic care often is indicated in these cases. Attempts to guess whether the back pain or the lower limb lameness is the primary root of the problem are often futile and biased. Whether a primary or secondary contributing factor, any clinically evident musculoskeletal dysfunction needs to be diagnosed individually and treated appropriately.

Primary presenting complaints related to the poor performance or other nonmusculoskeletal problems included refusal to canter, bucking only during a canter to the right, abnormal gait without any signs of lameness, shifting limb lameness, not tracking straight, lethargy, and bad behavior. In these cases, complete and sometimes extensive diagnostic evaluations are indicated. However, the diagnostic plan should begin with a manual therapy or acupuncture assessment to help direct the course of diagnostic tests performed. Unfortunately,

equine chiropractors or acupuncturists often are called in as a last resort for evaluation or treatment of vague, poor performance-related issues.

Chiropractic treatment was not provided in seven (14%) horses because of potential contraindications present at the time of assessment. Musculoskeletal conditions that could be aggravated with chiropractic care or were not appropriate chiropractic cases included confirmed static cervical myelopathy, cervical fractures, acute soft tissue infection and abscessation, residual neuromuscular disease (botulism), acute hind limb ataxia, and potential pelvic fracture. Further research is needed to assess the effectiveness and safety of chiropractic, acupuncture, and physical therapy modalities as adjunctive therapies to traditional veterinary care in these cases of overt musculoskeletal pathology.

Substantial need exists for specific and objective measures of musculoskeletal dysfunction not currently available in veterinary medicine. Several assessment tools currently utilized in the human field have a great potential for application to equine patients. Some of these include functional outcome measures that assess how well a horse is able to do the job asked of it, for example, its speed, flexibility, coordination, strength, and endurance. Quantitative assessments of pain include the use of a 0 to 10 pain scale, algometry or pain pressure threshold measurements, and mapping areas of pain. New insights into measuring musculoskeletal dysfunction hopefully will assist in assessing the effectiveness of many of the traditional and complementary modalities currently applied to horses with the rationale of reducing morbidity and improving overall performance.

Supplemental Readings

- Harman JC: Complementary (alternative) therapies for poor performance, back problems, and lameness. In Robinson NE (ed): *Current Therapy in Equine Medicine*, 4th edition, pp 131-137, Philadelphia, WB Saunders, 1997.
- Liebenson C: *Rehabilitation of the Spine: A Practitioners Manual*, Baltimore, Md, Williams & Wilkins, 1996.
- Porter M: *The New Equine Sports Therapy*, Lexington, Ky, Eclipse Press, 1998.
- Schoen AM: *Veterinary Acupuncture: Ancient Art to Modern Medicine*, 2nd edition, St Louis, Mosby, 2001.
- Schoen AM, Wynn SG: *Complementary and Alternative Veterinary Medicine: Principles and Practice*, St Louis, Mosby, 1998.

SECTION XI

Cardiovascular Disease

Edited by Dr. Mary M. Durando

CHAPTER 11.1

Cardiovascular Examination and Diagnostic Techniques

MARY M. DURANDO

Davis, California

LESLEY ELISSA YOUNG

Newmarket, Suffolk, United Kingdom

Cardiovascular abnormalities in the horse are not uncommon, and most equine clinicians have encountered them; however, their significance as a cause of overt clinical disease is not always clear. Horses have a high prevalence of both functional and pathologic murmurs and dysrhythmias. Furthermore, murmurs caused by underlying cardiac pathology do not necessarily result in signs of cardiac disease at rest, nor do they always noticeably decrease athletic performance. This makes determination of their significance difficult. After an abnormality is detected, the challenge to the equine clinician lies in making an accurate diagnosis, and perhaps most importantly, determining the significance of the abnormality for the immediate and long-term health of the animal and its future athletic performance. This requires a basic knowledge of the physiology and anatomy of the cardiovascular system and the ability to integrate clinical and diagnostic findings.

In cases of a cardiovascular abnormality, a thorough physical examination of the entire animal is important. Such an approach allows the clinician to determine the hemodynamic effects of any abnormality present and facilitates assessment of disease in other body systems that may have important secondary effects on the heart.

If primary cardiac disease is suspected after a thorough cardiovascular examination has been performed, other ancillary diagnostic aids may be necessary. Most commonly echocardiography is used to identify accurately the source of a problem and provide additional information about structural cardiac damage and secondary cardiac chamber enlargement. Electrocardiography enables the origin of an arrhythmia to be accurately determined and in many cases is also necessary to perform during appropriate ex-

ercise. Judicious use of these adjunctive diagnostic methods facilitates an accurate diagnosis and prognosis while simultaneously allowing arrhythmias and valvular and myocardial disease to be monitored.

Several other more technologically demanding and expensive tests of cardiovascular function are also available. These include techniques for measurement of cardiac output and other indices of systolic and diastolic ventricular function, measurement of aerobic and exercise capacity using treadmill exercise testing, and 24-hour continuous Holter monitor recording. However, most are available only in referral institutions and are reserved for special situations.

This chapter focuses on examination of the cardiovascular system and the adjunctive aids that can be used in the diagnosis and prognosis of suspected cardiac abnormalities.

HISTORICAL FINDINGS

A thorough history is critical when considering the significance of cardiac murmurs or dysrhythmias in horses. Although it is usually obvious when a patient is presented in overt heart failure, this is not the most frequently encountered clinical situation. More common is to discover a cardiac murmur or dysrhythmia incidentally in an otherwise healthy animal, during a prepurchase examination, in a horse presented with a history of poor performance, or in a sick horse with other nonspecific signs.

These are the situations in which the significance of a cardiac murmur is much more perplexing. For these reasons, a precise history is critical. The exact complaint of the owner and the duration of the complaint should be ascertained. A complete medical history also must be obtained. The horse is equipped with enormous cardiac re-

serve and therefore evaluation of the cardiovascular system at rest provides limited information. Only when increased demand is placed on the heart during exercise is the effect of more subtle lesions become obvious.

SIGNALMENT

The age, sex, and breed of the horse can be important in determination of the significance of auscultatory findings. Although vagally mediated dysrhythmias are common in Thoroughbreds and performance horses, they would be unusual in an aged child's pony. Similarly, the presence of a quiet diastolic murmur of aortic insufficiency in a horse under 10 years of age may warrant further investigation, whereas it may be of much less concern if it is detected in a 21-year-old schoolmaster. Consideration of current and future use of the horse also is important, including projected athletic demands, when determining the significance of cardiac abnormalities, particularly because resale value is a concern.

CLINICAL EXAMINATION

Although a thorough physical examination is a necessity, particular attention should be placed on the cardiovascular system.

Body Condition

Cardiac cachexia is an inevitable consequence of heart failure. It is often dramatic in onset, occurring within a short time of cardiac decompensation. It is usually most obvious in the highly muscled areas: for example, the hindquarters in mature conditioned horses or the neck and shoulder in young stock.

Peripheral Edema

Cardiac disease is one of the more rare causes of edema in horses. When cardiogenic edema is present, it occurs most commonly under the brisket, and even in severe cases, is often localized and can be overlooked easily. Cardiogenic edema of the lower limbs is rare even in acute heart failure. Thus when limb edema is observed in isolation, it is not likely to indicate cardiac dysfunction.

Pulse Quality

The peripheral pulse provides a window to the heart's function as a pump. It also may provide a clue to the severity of valve lesions picked up on auscultation. The facial artery provides a convenient site for examination of the peripheral pulse. First the heart rate and rhythm can be determined. A normal heart rate usually rules out congestive heart failure in cases of weight loss and general malaise. If a patient is in heart failure, its heart rate will be elevated above the normal expected value appropriate for the animal's type and fitness. These patients usually sustain their heart rates between 55 and 80 bpm depending on the type and severity of disease. Bradydysrhythmias also may result in low-output heart failure, so an abnormally low resting heart rate relative to breed and

fitness also may be noteworthy. Conversely congestive heart failure alone is unlikely to cause sustained heart rates of more than 100 bpm. In these cases, the presence of coexisting tachydysrhythmias is suspected.

Pulse quality reflects the difference between the systolic and diastolic blood pressure. The difference between the two, rather than the magnitude of either, is detected when the pulse is palpated. To obtain an estimate of mean arterial pressure, the amount of digital pressure needed to occlude the pulse must be assessed subjectively. The mean pressure provides an indirect indication of the heart's pumping ability, as follows:

$$BP = CO \times SVR$$

where *BP* is arterial blood pressure; *CO* is cardiac output; and *SVR* is systemic vascular resistance.

Once the compensatory mechanisms begin to fail, despite elevations in heart rate and intense vasoconstriction, arterial blood pressure no longer can be maintained. In these instances relatively little pressure is needed to occlude the peripheral pulse or it may be difficult to palpate at all. Although blood pressure and cardiac output also can be diminished for other reasons, most commonly in cases of hypovolemia resulting from massive fluid loss, these conditions are unlikely to be confused with cardiac failure.

Pulse quality also can reflect the severity or type of underlying disease. A characteristically bounding pulse (i.e., a wide difference between systolic and diastolic pressure) can be indicative of marked aortic insufficiency in older horses, or extracardiac left-to-right shunts in foals.

Other Indicators of Peripheral Perfusion

As described previously, acute cardiac failure results in low cardiac output and peripheral circulatory shut down to maintain vital organ perfusion. Poor peripheral perfusion is most easily detected in horses by palpation of the extremities, particularly the legs and ears. When the systemic circulation is severely compromised, these areas feel noticeably cold to the touch.

The interpretation of mucous membrane color is difficult in horses because it is so dependent upon ambient lighting conditions and is relatively nonspecific for a particular disease. Capillary refill times also must be interpreted with caution in this species because they too can reflect several different pathophysiologic processes.

Examination of Jugular Veins

Jugular Distention

The amount of filling of the jugular veins reflects the pressure within the right atrium. The higher the right atrial pressure, the greater is the vertical distance up the neck that the jugular veins are filled. Normal right atrial filling pressure (central venous pressure) can support a vertical column of blood one fourth to one third of the way up the horse's neck, provided the neck is relaxed in a normal position. Above this level, the veins collapse under the effects of gravity. Pulsations in the jugular vein are seen only in the filled portion (lower one fourth to one third).

The two jugular veins can be considered as a U tube connected directly through the right atrium. The vertical height of blood inside is dictated by right atrial pressure. If the horse's head is lowered while right atrial pressure remains the same, blood will fill the veins further up the neck. Similarly if this U tube is tilted towards the horizontal from vertical, fluid also will travel along both arms of the U, but the vertical distance of the end of fluid from the reference level does not change. This has an important clinical application: it is important not to overinterpret jugular distention. The clinician must make sure that any alteration in jugular filling is evident only when the horse's head is in the normal upright position.

Normal Jugular Pulsations

The largest pulse visualized is caused as right atrial pressure increases and subsequently falls when the atria contract immediately before ventricular systole. The second wave occurs soon after, as the tricuspid valve balloons back into the atrium during isovolumic ventricular systole. This second pulse coincides with and summates with the referred pulse in the underlying carotid artery. As the base of the heart is pulled downward during the remainder of systole atrial pressure falls. The pressure then starts to rise again as the right atrium fills (third wave), until the AV valve opens at the start of diastole. Although the first pulsation wave is invariably visible, observation of the other two pulses depends on central venous pressure.

Effect of Disease on Jugular Filling and Pulsations

In general, confusion exists over not only what causes jugular pulsations and their significance but also the effects that disease might have on them. Often people have expectations that the jugular pulses are pathognomonic for particular cardiac conditions. In general, though, the changes in these pulsations are rarely as obvious as the textbooks would have us expect, so changes in them may be difficult to interpret.

Congestive Heart Failure

As right atrial pressure becomes increasingly elevated during right congestive heart failure, the jugular vein becomes filled further up the neck. In severe cases, the jugular vein is distended up to the level of the mandible. This also occurs in cranial caval obstruction, pericardial effusion, and restrictive pericarditis.

Tricuspid Regurgitation

When the tricuspid valve is incompetent, blood is ejected in a retrograde fashion into the right atrium during ventricular systole. This causes an elevation in right atrial pressure and should cause a jugular pulsation, with the magnitude dependent upon the severity of regurgitation. If the jugular vein is occluded and the blood milked out downwards to the heart, in cases of severe tricuspid regurgitation the vessel refills with regurgitant blood from the right atrium.

Atrial Fibrillation

Theoretically in atrial fibrillation the largest wave resulting from atrial contraction is absent, whereas the third "filling" wave should be augmented. This is much less easy to

spot in practice, because timing of jugular pulse waves is usually not well developed. The most striking abnormality should be the irregular irregularity of the pulses.

Low-Output Cardiac Failure

If the jugular vein is completely occluded it should fill proximal to the occlusion within a few seconds. Reductions in central venous pressure occur most commonly because of hypovolemia, but jugular filling also may be reduced in cases of severe left-sided heart failure, when as a result of low cardiac output, venous return is depleted.

Atrioventricular Dissociation

In cases of total third-degree atrioventricular (AV) block, or AV dissociation, when the ventricles are contracting completely independently of the atria, sometimes the atria contract against a closed AV valve (during ventricular systole). This causes large increases in right atrial pressure, and the pulse waves appear to shoot up the jugular veins to the mandible like a cannon ball. One relatively common presentation of AV dissociation that may result in jugular pulsations is rapid ventricular tachycardia. Complete third-degree AV block is extremely rare in horses.

Pulmonary Edema

Alveolar and interstitial edema can occur as a consequence of marked elevations in left atrial pressure, as a result of severe left-sided heart failure. Thoracic auscultation frequently is disappointing in these patients, even though pulmonary edema is known to be present. In severe cases, large quantities of white, frothy edema fluid passes down the nose, yet even then, thoracic auscultation may fail to reveal convincing evidence of the textbook crackles that indicate edema in other species. More frequently, tachypnea, increased bronchovesicular sounds, and nostril flair are noted. The increased respiratory rate that always accompanies severe alveolar edema is the most reliable method for detecting pulmonary congestion in horses. Thoracic radiography is also helpful to confirm alveolar fluid accumulation and monitor diuresis. Increased pulmonary density is usually most marked on the cardiophrenic angle. Coughing is not a feature usually noted with early interstitial pulmonary edema in horses, unless secondary bacterial infection is present.

Cardiac Auscultation

Despite advances in ultrasound technology, cardiac auscultation remains the most important technique for the diagnosis of cardiac disease in horses. Therefore developing a systematic, logical approach to cardiac auscultation is important, if it is to yield maximal results. The findings obtained by cardiac auscultation must then be used in combination with performance history, patient details, and clinical examination to evaluate the significance of cardiac disease.

Auscultation must be performed in a quiet environment free from distractions, and to be effective, the examiner must have knowledge of the cardiac cycle and the origins of both normal and abnormal heart sounds. A sys-

tematic approach is critical and the entire cardiac area on both sides of the chest always should be examined.

Technique

Palpation of the cardiac impulse (medial to the left elbow near the left ventricular inflow) is useful before auscultation begins. This area is referred to as the *apex beat* and is the main reference point for auscultation of the valves. It also may give an indication whether the heart is either enlarged or displaced caudally. The mitral valve is ausculted in the area of the apex beat, or slightly dorsal to the point of the elbow, in the fifth intercostal space just behind or medial to the triceps muscles. The aortic valve is best heard dorsal and more cranial to the apex beat in the fourth intercostal space. The pulmonic valve requires more effort to auscult because it is cranial and ventral to the aortic valve in the third intercostal space. Occasionally, in foals or small thin horses, murmurs of tricuspid regurgitation can be heard cranial to the pulmonic valve in the second intercostal space. However, the tricuspid valve is much more easily examined from the right side, medial to the triceps, in the fourth intercostal space.

Normal Heart Sounds

Between two and four heart sounds can be heard during auscultation of normal horses. It may not be possible to hear all four sounds in every horse. Review of the normal heart sounds and what causes them is important before considering cardiac murmurs.

First heart sound (S_1). S_1 and S_2 are the traditional “lub-dub” heard in all species. S_1 marks the onset of mechanical systole and ventricular ejection and is caused by the initial movement of the ventricles, closure of the AV valves and opening of the semilunar valves, with sudden acceleration and deceleration of blood. One of the components of the sound is associated with AV valve closure, so, as would be expected, the sound is heard most loudly around the mitral and tricuspid valve areas. It occurs at the same time as the apex beat. The first heart sound is usually longer, louder, and lower pitched than the second heart sound. S_1 can vary in intensity with premature contractions, atrial fibrillation, and ventricular tachycardia.

True splitting of S_1 is extremely rare. Splitting is much more commonly confused with the atrial sound S_4 , occurring in close apposition to S_1 . This effect produces the characteristic “le-lub” sound, heard when the chest is auscultated around the area of the apex beat.

Second heart sound (S_2). The second heart sound is best heard more dorsal and cranial to the apex beat, or the point of maximal intensity of S_1 . This coincides with the area over the aortic and pulmonic (semilunar) valves. S_2 results mainly from vibrations caused by the sudden reversal of blood flow as the outflow valves close and marks the onset of diastole.

Close splitting of S_2 occurs commonly but is heard only when a deliberate effort has been made to auscultate far cranial on the left thorax, over the pulmonary valve. Splitting occurs when the aortic valve closes before the pulmonic valve. Valve closure can be altered by changes in venous return, or intrathoracic pressure during respiration. Marked splitting is reported to be more prevalent in horses with pulmonary hypertension and chronic respira-

tory disease. Although splitting can be heard in association with recurrent airway obstruction (RAO), it is certainly not pathognomonic for the condition.

Third heart sound (S_3). The third sound is the one that causes the most difficulty when first becoming comfortable with cardiac auscultation. This arises probably because inexperienced auscultators expect it should be heard clearly in every horse, which is not true. It is best heard around the cardiac apex, slightly ventral to the point of maximal intensity of S_1 , or slightly dorsal and caudal to it. S_3 occurs soon after S_2 . It corresponds to the end of rapid ventricular filling as the ventricle becomes maximally distended by the inflow of blood. The vibrations that make up S_3 are usually of low frequency, so generally, in resting horses the sound is quieter than S_1 and S_2 . S_3 is the most variable of the heart sounds and is affected by heart rate. During exercise, as diastole shortens, less time exists for passive filling of the ventricle so that S_3 and S_4 tend to summate. The resultant sound is much louder (of similar volume to S_1 and S_2). When this gallop, or three-beat, rhythm is first heard, it can be confusing. In contrast to the situation in other species, the presence of a gallop rhythm in horses is not usually indicative of cardiac dysfunction because three-time rhythms occur not infrequently at elevated heart rates, for example, after exercise.

S_3 is also louder at resting heart rates in cases of enhanced ventricular filling or poor ventricular compliance, such as occurs in severe AV valve regurgitation and left ventricular volume overload. In these situations, the presence of a loud S_3 may well be another useful marker to the severity of underlying valvular or heart disease.

Fourth heart sound (S_4). S_4 is heard best in the area of the heart base (cranial and dorsal to the apex beat). It is composed of two sets of vibrations arising from active atrial contraction. It is thought that blood flow per se, although contributing to the sound, causes vibrations that are rarely audible. Instead, the main audible vibrations are associated with (1) transient snapping closed of the AV valves, as they are drawn together by the “venturi-like” effect of transvalvular flow, and (2) sudden vibrations caused by the walls of the ventricle, as their limits of distensibility are reached.

The PR interval dictates how easily audible the fourth sound is. Most commonly it is almost inextricably linked to S_1 , producing the characteristic “lelub” sound. The sound is fairly loud, although often it is masked by its close proximity to S_1 . S_4 can often be heard in isolation, before the blocked beats of second-degree block. S_4 is absent in cases of atrial fibrillation.

Abnormal Adventitious Sounds: Heart Murmurs

Auscultation of the heart first should involve determination of the resting heart rate and rhythm. If the rhythm is irregular, simultaneous palpation of an arterial pulse for pulse deficits may be informative. Once heart rate has been determined, careful auscultation for the presence of adventitious sounds should be performed at each valve area.

Murmurs are prolonged audible vibrations during a normally silent period of the cardiac cycle. Various ways of describing murmurs, including timing, duration, intensity, shape, quality, and point of maximal intensity, commonly

are used to help determine their significance and to communicate findings to others. Timing describes when in the cardiac cycle the murmur occurs, and is referred to as systolic, diastolic, or continuous. It may sometimes be necessary to palpate the peripheral pulse while auscultating to determine the timing of some murmurs. Duration is the length of the cardiac cycle occupied by the murmur (early, mid, late, holo, or pan). Intensity is described on a grade scale from grade 1 to either grade 5 or 6. Although the intensity of the murmur does not necessarily correlate with its severity, in general a loud coarse murmur with a palpable precordial thrill is likely to have more significance than a soft murmur early in the cardiac cycle. The shape describes the change in intensity of the murmur over time. This is typically caused by pressure differences between the chambers. A crescendo murmur usually increases in intensity in the early to mid portion of the cycle (ejection-type murmur), a decrescendo murmur decreases over time because of a lessening of the pressure difference between the chambers, and a plateau or band-shaped murmur stays a constant intensity throughout the cycle. Quality describes the characteristics of the sound such as soft, blowing, harsh, coarse, musical, or honking. Typically, musical murmurs are caused by a structure vibrating in the regurgitant blood flow, such as a flailing or fenestrated valve leaflet or a ruptured chordae tendineae. The location at which the murmur is heard best is called the *point of maximal intensity* (PMI). In general murmurs radiate along the direction of the abnormal blood flow. A widely radiating murmur is likely to reflect more severe regurgitation and a more severe lesion. The PMI of a murmur is described commonly with reference to the valve areas.

In addition to murmurs, other types of sounds such as squeaks, clicks, or rubs should be noted. Pericardial friction rubs can be mistaken for murmurs or pleural friction rubs if not critically evaluated. Although they have a similar rubbing or creaking sound as pleural friction rubs (distinct from murmurs), they are usually triphasic in nature and occur in relation to the cardiac cycle. Heart sounds are also likely to be muffled with pericardial effusion.

Finally, a complete examination also should include thorough auscultation examination of the pulmonary system because significant cardiac disease (i.e., left heart failure) can cause pulmonary edema and may be associated with secondary respiratory infection. More commonly, as respiratory disease is more frequently associated with coughing and poor performance than cardiac disease in horses, a thorough examination of the lungs and upper airways usually is required to rule out the presence of respiratory disease.

DIAGNOSTIC AIDS

Once evaluation of the cardiac system is complete, ancillary diagnostic aids may be deemed necessary to diagnose the problem specifically, to assess the abnormality during exercise, and to help formulate a treatment plan and prognosis. Although various ways of evaluating cardiac function exist and are being refined continuously, some of these are invasive and require sophisticated equipment and advanced training to interpret the data. This section concentrates on the most commonly used and widely available modalities.

Electrocardiography

Diagnosis of arrhythmias has been enhanced greatly by improvements in technology that allow electrocardiographic (ECG) recordings to be taken readily. ECG technology based on palm top computers is already available in the United Kingdom and is becoming increasingly affordable for equine practitioners. This newer technology is both portable and allows high quality recordings to be taken from exercising horses. The availability and practicability of these newer devices means that abnormalities of cardiac rhythm are diagnosed more frequently in horses at rest and during exercise and therefore that the significance of these abnormalities must be determined.

Irregularities in cardiac rhythm or an abnormal cardiac rate detected on physical examination always warrant further investigation by ECG. Several detailed accounts of the principles of electrocardiography in horses have been written, but it is beyond the scope of this section to review the topic in detail. Instead the principles needed to facilitate accurate interpretation are reviewed.

An electrocardiogram is a recording of the changes in the electrical potential difference of the heart plotted against time. These changes occur during depolarization and repolarization of the myocardium, and because the body is a conducting system, this electrical activity can be recorded on the body surface. In horses the base-apex lead is used most commonly to record the electrocardiogram. This lead system produces large complexes, which are easy to identify and are less affected by movement artifacts than the limb leads. In horses, ECGs are used primarily for detecting rhythm disturbances and monitoring cardiac rhythm over time and in response to drug therapy or exercise. Because of the anatomy of the equine conduction system, it is not a useful method for detecting ventricular enlargement or other structural abnormalities.

To record a base-apex lead, the (+) left arm electrode is positioned on the left hemithorax at the level of and just caudal to the olecranon (left cardiac apex), and the (−) right arm electrode is placed at the top of the right scapular spine near the withers, or two thirds of the way down the jugular groove on the right. The third electrode (ground) is placed in a remote position away from the heart. The ECG is recorded from lead 1 on the ECG machine. A schematic, representative base-apex ECG is shown in Figure 11.1-1. Good electrical contact is important, which can be improved with electrode paste or alcohol. Every effort should be made to remove interference from outside electrical objects and to reduce motion because these can cause artifacts that make accurate interpretation difficult. Some horses tolerate crocodile clips poorly, so in their place adult silver/silver chloride adhesive electrodes can be used. These produce good quality traces with minimal movement artifact. A multichannel ECG is rarely needed. In general, equine ECGs use a paper speed of 25 mm/sec and a calibration 1 cm/mV, but the calibration may be adjusted to optimize complex size.

A systematic approach is necessary to evaluate an ECG. The P wave reflects atrial depolarization, the QRS complex ventricular depolarization, and the T wave ventricular repolarization. The equine P wave is frequently biphasic, with both portions positive or occasionally a negative/positive

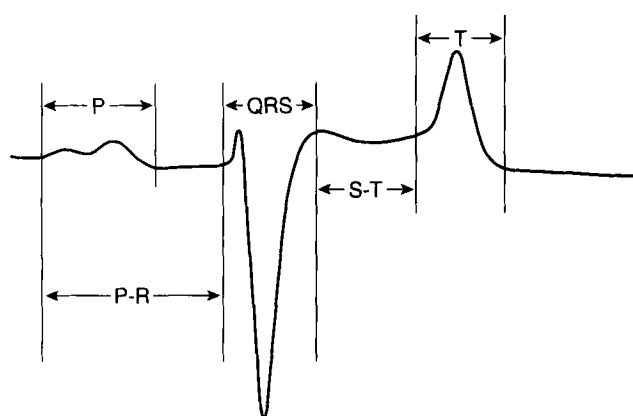


Figure 11.1-1 Schematic representation of a base-apex electrocardiogram (ECG) in the horse. The various waves, segments, and intervals are labeled for clarity. Note the bifid P wave (normal).

configuration. The QRS is negative in a base-apex lead, whereas the T wave can be negative, positive, or biphasic.

Analysis of the Electrocardiogram

Assessment of electrocardiogram quality and instrument settings. Attempting to interpret a trace that is not of diagnostic quality is futile. Most recorders print the instrument settings to allow cardiac complexes and events to be measured accurately.

Calculation of heart rate. This can be obtained by counting the number of complexes in a 6-second strip and multiplying this number by 10. However, just as it is unreliable to determine the pulse rate from a 6-second examination, calculation of the heart rate from a longer time strip gives improved accuracy. This is especially true when the heart rate is low or an irregular arrhythmia occurs. Alternatively heart rate can be calculated by dividing 60 by the R-R interval in seconds.

Determination of the P:QRS ratio. Is there a P wave for every QRS complex and a QRS complex for every P wave? Both the ventricular and the atrial rate should be calculated if a ratio of other than 1:1 exists.

Determination of the predominant rhythm. Inspection of the regularity of the P waves and the QRS complexes indicates if a dysrhythmia is present. The R to R and P to P intervals should be regular, with consistent PR and RP intervals. The P waves and QRS complexes should be similar to each other in configuration, with particular attention paid to the QRS complex. Variations may indicate ectopic beats or abnormal conduction patterns.

Measurements

ECG traces in horses normally are recorded at a paper speed of 25 mm/sec. At this speed each small vertical box represents 0.1 millivolt and each small horizontal box represents 0.04 seconds (40 milliseconds). Reference values for the various time intervals are as follows:

P height: 0.15 Volts; duration 0.12 to 0.14 seconds
 P-R interval: 0.36 to 0.56 seconds
 QRS duration: 0.1 to 0.12 seconds
 Q-T interval: <0.6 seconds

For intermittent or paroxysmal arrhythmias a 24-hour continuous recording ECG (Holter monitor) may be necessary. Because sympathetic stimulation is a potent arrhythmogenic stimulus, assessment of the effect of appropriate exercise on the abnormal focus or rhythm is necessary in almost all cases of equine arrhythmias. This allows a more accurate prognosis to be provided for future athletic ability and a rational decision to be made about the horse's safety for a rider.

Telemetric ECG recorders rely on transmission of the ECG signal by radiowaves to a distant monitor. Although effective, these systems are expensive and as such tend to be restricted to referral institutions unless purchased second hand. In the United Kingdom, the more recent development of a bipolar recording system interfaced to a palm-top computer now allows resting and exercising traces to be obtained from horses cheaply and simply in field conditions. For both types of recordings, the standard base-apex lead configuration is amended so that the electrodes are placed on the left scapula and caudal to the girth area on the left, where they are accessible to the rider and minimally affected by movement. A spare electrode can be placed in each location so that the rider can reattach the electrode should one become dislodged. An example of the effect of exercise on an arrhythmia at rest, using a bipolar recording system interfaced to such a computer is shown in Figure 11.1-2. Specific arrhythmias are addressed in a later chapter.

Echocardiography

Echocardiography is indicated for evaluation of murmurs, potential congenital defects or unexplained cyanosis in neonates, dysrhythmias, exercise intolerance, muffled heart sounds (potential pericardial disease), suspected myocardial dysfunction, suspected abnormalities of the great vessels, unexplained fever, unexplained collapse, or congestive heart failure. Once a specific diagnosis has been made, monitoring progression of the disease and response to treatment is useful. For the information obtained from the echocardiogram to be properly interpreted, a basic knowledge of the principles of ultrasound and its application in the horse is necessary. Improper or inappropriate views can lead to erroneous conclusions or misdiagnoses. Standardized image planes are necessary for a methodical approach so that abnormalities are not missed; they are also important for serial comparisons and comparisons among different examiners.

Numerous comprehensive descriptions of the physics of ultrasound exist and therefore are mentioned only in a brief review here. Echocardiography uses high frequency sound waves that travel through the heart and are absorbed, reflected, or refracted as they meet blood and tissue interfaces. This allows visualization of internal architecture. The waves reflected back to the transducer are responsible for the displayed image; different tissue interfaces reflect different amounts of ultrasound. Diagnostic ultrasound uses high-frequency sound waves (2-10 MHz). Frequency is inversely proportional to wavelength, therefore lower frequencies have a longer wavelength. Attenuation of the ultrasound beam occurs at a rate proportional to both tissue depth and frequency, so lower frequency

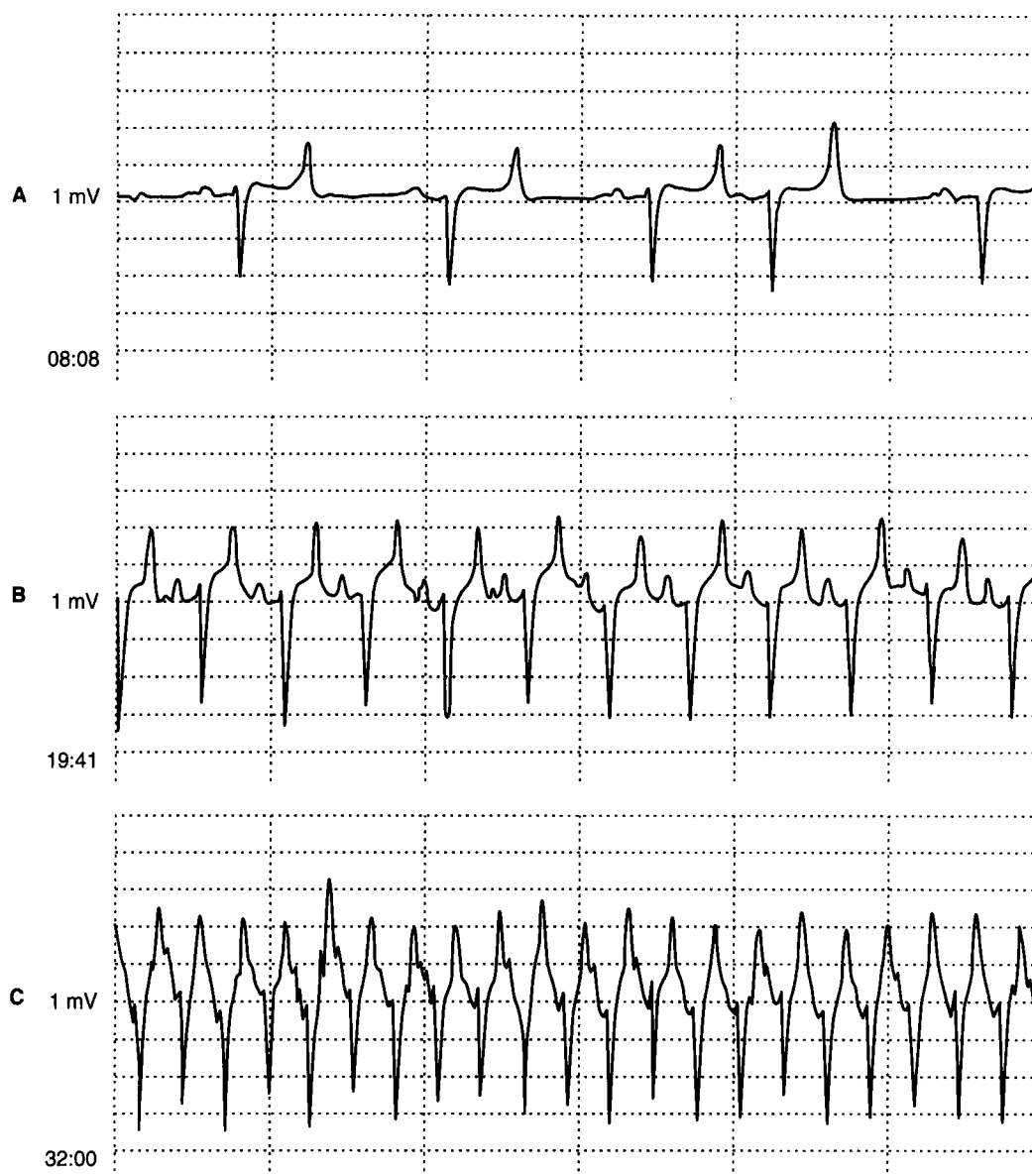


Figure 11.1-2 Electrocardiogram (ECG) showing the effect of exercise on an arrhythmia. **A**, Resting base-apex ECG from a 7-year-old Thoroughbred with an obvious arrhythmia at rest. Note the single atrial ectopic beat (fourth complex) followed by a normal P-P interval. The ectopic beat has a slightly different shape; unlike the sinus beats, it is not bifid. **B**, With exercise the ectopic focus is overridden, as shown in this trace from the same horse taken during trotting (heart rate = 110). The R-R interval is constant, and P waves are still visible, distinct from the preceding T waves. **C**, At very fast heart rates (e.g., heart rate = 232) the P wave becomes increasingly difficult to discern because it is now buried in the preceding T wave, but the R-R interval is absolutely regular.

probes penetrate further. In contrast, higher-frequency probes have shorter wavelengths, which give better detail (improved lateral resolution) but cannot penetrate tissues deeply.

Evaluation of adult equine hearts usually requires a sector scanner operating at a low frequency (2-3.5 MHz) with a displayed depth of 30 cm. Foals may be imaged with higher-frequency probes. When low frequency probes are used, their depth of penetration more than compensates the poorer lateral resolution. Two methods of displaying

images are used: two-dimensional (2-D) or real time B-mode (brightness) and M-mode (motion mode). Doppler echocardiography is used to evaluate intracardiac and valvular blood flow. The three techniques are complementary, and all are necessary to perform a complete examination, particularly in the investigation of a murmur.

Two-Dimensional Echocardiography

The ultrasound beam mechanically or electronically sweeping in an arc over the tissue creates 2-D images. These im-

ages are rapidly updated (high frame rates) to allow a real time image. 2-D images can be swept over multiple image planes and give the best information when evaluating the relationship between great vessels and chambers, cardiac structure, chamber size, myocardial function, and valve appearance and function. Any abnormalities of structure, such as wall thickness, myocardial and valve echogenicity, and symmetry, and of function such as movement of valves and walls, can be evaluated. The overall size and location of the heart also can be assessed.

Motion Mode Echocardiography

M-mode imaging is a one dimensional "ice-pick" evaluation of the heart. It depicts the cardiac structure in question along the y-axis, over time presented on the x-axis. The simultaneously displayed ECG permits accurate timing relative to the cardiac cycle. Its high sampling rate gives superior resolution of rapidly vibrating structures. It is also extremely useful for measurements of chambers, particularly the left ventricle, and evaluating ventricular function—that is, fractional shortening. The M-mode cursor is positioned optimally using the 2-D image. The best quality 2-D and M-mode images are obtained if the highest frequency that penetrates adequately is used and the ultrasound beam is perpendicular to the structures being evaluated.

Doppler Echocardiography

Doppler echocardiography is a sensitive technique for the detection of abnormal blood flow, and can detect valve dysfunction in its earliest stages. "Doppler" echocardiographic methods estimate the velocity of moving red blood cells (RBCs) using the shift in frequency between the transmitted and received ultrasound wave that occurs when a sound wave is reflected off the RBCs. When the cells are moving towards the transducer, the reflected frequency is higher than the transmitted frequency. The converse is true when the cells are moving in the opposite direction. In pulsed and continuous wave Doppler echocardiography, blood flow velocity is displayed along the y-axis versus time on the x-axis, and the direction is shown relative to the baseline. Unlike 2-D and M-mode, Doppler echocardiography, is best performed with the ultrasound beam parallel to blood flow (<20-degree angle), otherwise velocity of blood flow is significantly underestimated. Again, lower frequency probes are advantageous because they are capable of detecting higher velocity blood flow at a greater depth. Doppler echocardiography is used for several purposes, including measurement of blood flow velocities across valves, differentiation of laminar and turbulent flow, detection and semi-quantitation of disturbances in blood flow from both congenital and acquired lesions, and estimations of diastolic and systolic ventricular function. All Doppler techniques generally are performed under 2-D guidance.

Pulse wave (PW) Doppler is a method of detecting blood flow in discrete regions within the heart. It uses individual sampling gates placed by the examiner to interrogate specific areas of interest. Pulses of ultrasound are transmitted to the area of interest at a fixed frequency (the pulse repetition frequency) that allows them to be received before the next one is sent out. This allows precise

localization of flow but greatly limits the maximum velocity that can be detected. When blood flow velocity exceeds the Nyquist velocity, which is one-half the pulse repetition frequency, the signal aliases, or wraps, around the baseline, preventing accurate resolution of its direction and magnitude. PW usually is done in conjunction with 2-D echocardiography to guide the examiner to specific locations to place the sampling gates. PW can localize accurately the area of abnormal blood flow but cannot resolve high velocity blood flow above the Nyquist limit.

In contrast, continuous wave (CW) Doppler can resolve accurately the peak velocity of blood flow. With this modality ultrasound waves are continuously transmitted and received. The disadvantage lies in its inability to accurately localize the origin of any abnormal flow as velocity is detected along the entire path of the ultrasound beam. Because it accurately can record high velocities, CW Doppler is used most often to estimate pressure differences between chambers, for example, across the mitral valve or a septal defect, using the peak velocity of the regurgitant jet. Pressure gradients can be derived from a modification of the Bernoulli equation, as follows:

$$\text{Pressure gradient} = 4V^2$$

(V = Peak velocity of flow between the two chambers)

This principle is useful to evaluate the hemodynamic significance of ventricular septal defects and mitral regurgitation and to detect pulmonary hypertension using the velocity of the resultant tricuspid valve regurgitation.

Color flow Doppler is a sophisticated form of PW Doppler and is most useful to screen large areas of abnormal flow. It uses multiple sample gates in a targeted area to detect blood flow. Each small sample volume is then color-coded to represent the motion of the blood flow in the selected area. Flow direction, velocity, and its characteristics (turbulent or laminar flow) can be depicted. This color-coded image is displayed overlying either a simultaneously derived 2-D (for location) or M-mode (for accurate timing) image. It is similar to PW, except use of multiple gates allows large areas of the heart and vessels to be screened for abnormal flow. By convention, flow coded red is directed toward the transducer and flow coded blue is away from the transducer. Usually, the higher the flow velocity, the lighter the color, and turbulent flow (e.g., regurgitant flow) is colored green. Because color flow Doppler is a pulsed technique aliasing also occurs but can readily be identified from the abrupt transition from the paler shades red to blue or vice versa, even though the direction of flow has not changed.

Contrast Echocardiography

Contrast echocardiography involves injection of microbubbles into the circulatory system and assessment of their path through the heart. Either selective (in specific cardiac chambers) or nonselective (jugular vein) injections are used. A crystalloid, often mixed with the patient's blood and agitated strongly to facilitate bubble formation, is used. The microbubbles, which appear echogenic in the hypoechoic blood, do not pass through the lungs and therefore are not visible in the left heart unless a right-to-left shunt is present or the injection was made into the

left heart. A filling defect (negative contrast) can be seen when a shunt from left to right exists. In the absence of color flow and Doppler techniques, contrast echocardiography was used for evaluating tricuspid regurgitation, complex congenital abnormalities, and/or septal defects. Because color flow Doppler has become readily available, contrast echocardiography rarely is required.

Basic Scanning Technique

Proper technique and display of images is essential for interpretation of the echocardiogram. Several comprehensive articles on standardized images in the horse have been published. A brief description of 2-D and M-mode echocardiography is given here. However, for more detail, and for techniques of Doppler echocardiography, the reader should consult this chapter's readings list. Standardized images have been developed that permit comparison of serial examinations over time and allow meaningful comparisons among different clinicians and researchers. This facilitates comparison of data between individuals and the development of normal values. Mistakes in probe placement and the views obtained easily can lead to erroneous conclusions or significant omissions. Images are referenced to intracardiac landmarks rather than external transducer positions because of variation in the physical characteristics of individuals. However, for the purpose of learning the technique of echocardiography, the general placement of the probe is similar between horses for the same views, with minor adjustments in rotation and angulation. The examination should be performed in a systematic manner to avoid overlooking abnormalities and arriving at premature conclusions. An ECG always should be displayed simultaneously for accurate timing.

The examination should begin on the right side of the horse. In the majority of normal horses the entire heart fits on a 30-cm screen. A machine capable of penetrating this depth is preferable because visualization of the entire heart on the screen allows better assessment of the relative size of the chambers and great vessels and their relationship to each other. Most of the conventional views are obtained from the right side, although examination from the left side is also needed when a left-sided murmur (suspect mitral or aortic regurgitation) exists, the entire heart cannot be visualized from the right, or to allow alignment with aortic and mitral blood flow for Doppler echocardiographic techniques.

The right side is imaged in the fourth intercostal space midway between the point of the shoulder and the olecranon where the heart is not overlain by lung. Depending on the individual horse's anatomy, this is facilitated by placement of the right forelimb forward. In general, three long axis and three short axis views are obtained from the right side, and these are optimized by subtle changes in transducer angulation and rotation. M-mode and Doppler echocardiographic examinations are facilitated using these standard 2-D views.

The standard echocardiographic 2-D and M-mode views are shown in Figures 11.1-3 to 11.1-5. The right ventricular outflow tract (RVOT) view is obtained by angling the transducer slightly cranial and dorsal towards the left point of shoulder, with the scan marker dorsal (Figure 11.1-3, A). The right atrium and ventricle, tricuspid valve,

pulmonic valve, pulmonary artery, and aorta are visible in this view. For the left ventricular outflow tract (LVOT), the transducer should be angled straight across the chest and rotated slightly clockwise, to about the one o'clock position (Figure 11.1-3, B). In this view the right atrium and ventricle, tricuspid valve, interventricular septum, left ventricle, aortic valve, aorta root, left atrial appendage, and a portion of the pulmonary artery are visualized. The long axis four-chamber view is obtained by angling the probe caudally with the scan marker dorsal (Figure 11.1-3, C). This view shows the left and right atria, the left and right ventricles, the tricuspid valve, the mitral valve, the interventricular septum, and the left ventricular free wall.

The short axis views are best obtained with the transducer scan plane rotated to approximately 4 o'clock. As the transducer is angled from ventral to dorsal the apex of the left ventricle and papillary muscles, the chordae tendineae, mitral valve, aortic valve cusps and aortic root are seen (see Figure 11.1-4). The transducer may need to be angled slightly cranially and rotated slightly clockwise to optimize the aortic valve. For all views, slight changes in angulation, rotation, or position may be needed to optimize the image, depending on the physical characteristics of the horse.

M-mode measurements are obtained from the short axis views by perpendicularly bisecting the chamber with the cursor. M-mode images are used to measure ventricular chamber size and wall thickness and to calculate indices of ventricular function including fractional shortening (FS) and ejection fraction. LV and RV diameters in systole and diastole, LV free wall thickness in systole and diastole, septal thickness in systole and diastole, aortic root diameter in diastole, left atrial appendage diameter in systole, and maximal opening of the mitral valve are measured from M-mode images (see Figure 11.1-5).

The FS, expressed as a percent, is calculated from the LV view just below the mitral valve at the chordal level. It is the difference between the LV diameter at end diastole and peak systole, divided by the end diastolic LV diameter, multiplied by 100 and gives an indication of contractility of the heart, as follows:

$$FS = \frac{LVIDd - LVIDs \times 100}{LVIDd}$$

These indices are generally combined with measurements of chamber size and Doppler assessment of valve function to assess the function of the equine heart and the hemodynamic significance of any flow disturbances or anatomical defects present.

The left side is imaged in the third, fourth, and fifth intercostal spaces midway between the point of the shoulder and the olecranon. From this side, the left atrium, mitral valve, left ventricle, aorta, and pulmonary artery are evaluated most commonly. The left atrium and ventricle can be visualized in long axis, allowing measurement of the left atrial diameter and assessment of the mitral valve (Figure 11.1-6). This view is best imaged in the fifth intercostal space. The left ventricular outlet, aorta, and aortic valve can be visualized in the fourth intercostal space. These views allow better alignment with blood flow across

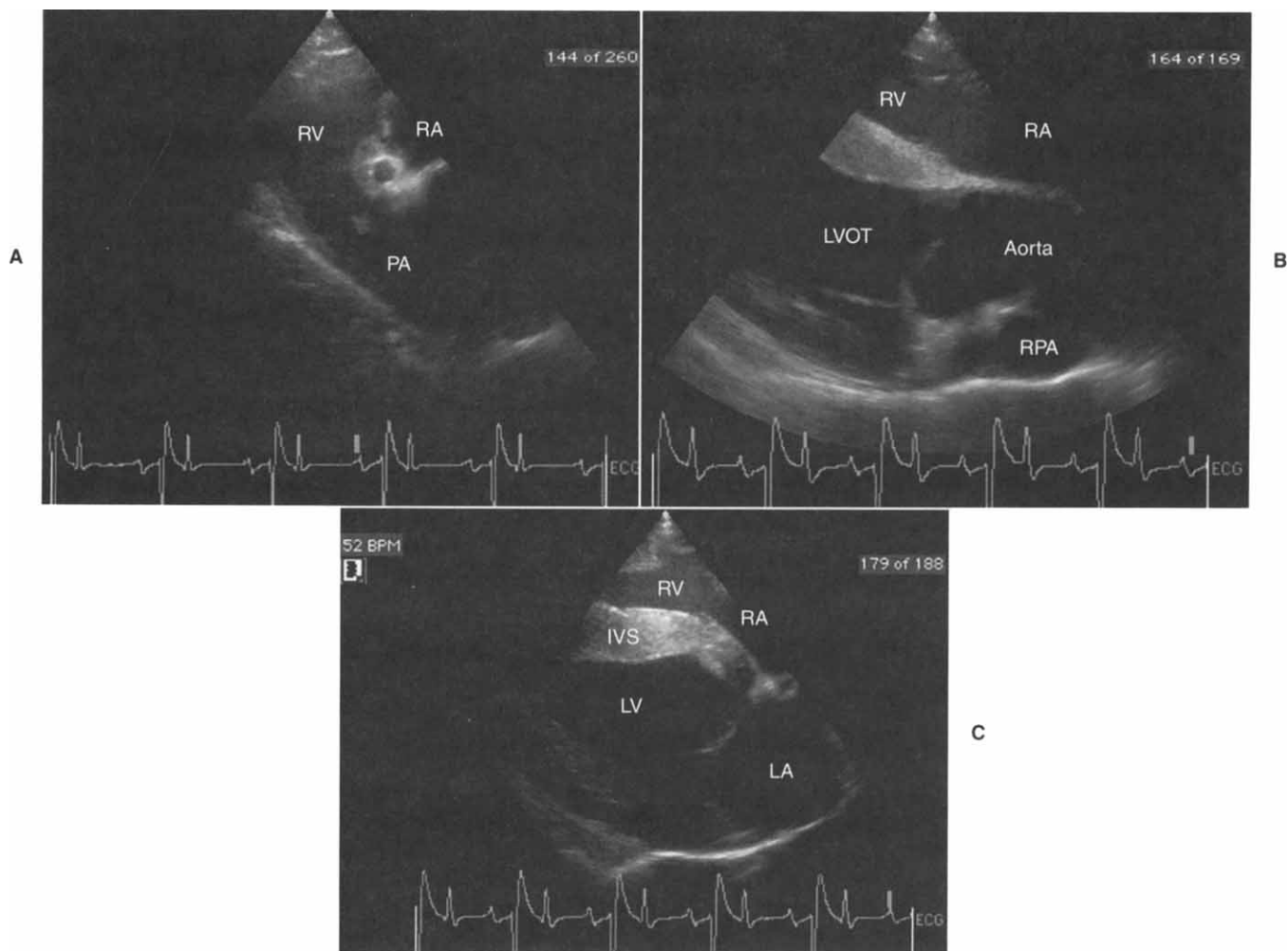


Figure 11.1-3 Standard long axis echocardiograms from the right side. **A**, Right parasternal two-dimensional (2-D) echocardiogram of the right ventricular outflow tract. This image is useful to view the pulmonic valve, to measure the diameter of the pulmonary artery, and to record pulmonary outflow velocities by Doppler echocardiography. *RA*, Right atrium; *RV*, right ventricle; *PA*, pulmonary artery. **B**, Right parasternal 2-D echocardiogram of the left ventricular outflow tract (aorta). The aortic valve is evaluated in this view, and measurement of the diameter of the aorta to calculate cardiac output is performed from this image. Membranous ventricular septal defects (VSD), the most common location for a VSD, can be visualized, and the velocity of flow through the VSD can be measured by Doppler echocardiography to assess its hemodynamic significance. Aortic aneurysms also can be seen, and the extent of tricuspid regurgitation can be assessed by Doppler echocardiography. *RA*, Right atrium; *RV*, right ventricle; *LVOT*, left ventricular outflow tract; and *RPA*, Right pulmonary artery. **C**, Right parasternal four-chamber view, showing the right and left atria and ventricles. The relative size of the chambers can be assessed, as can movement of the septum and posterior free wall. Muscular VSDs also may be visualized in this view. *RA*, Right atrium; *RV*, right ventricle; *IVS*, interventricular septum; *LA*, left atrium; *LV*, left ventricle. (Courtesy Dr. Karen J. Blissitt, Midlothian, United Kingdom, and Dr. Lesley E. Young, Newmarket, United Kingdom.)

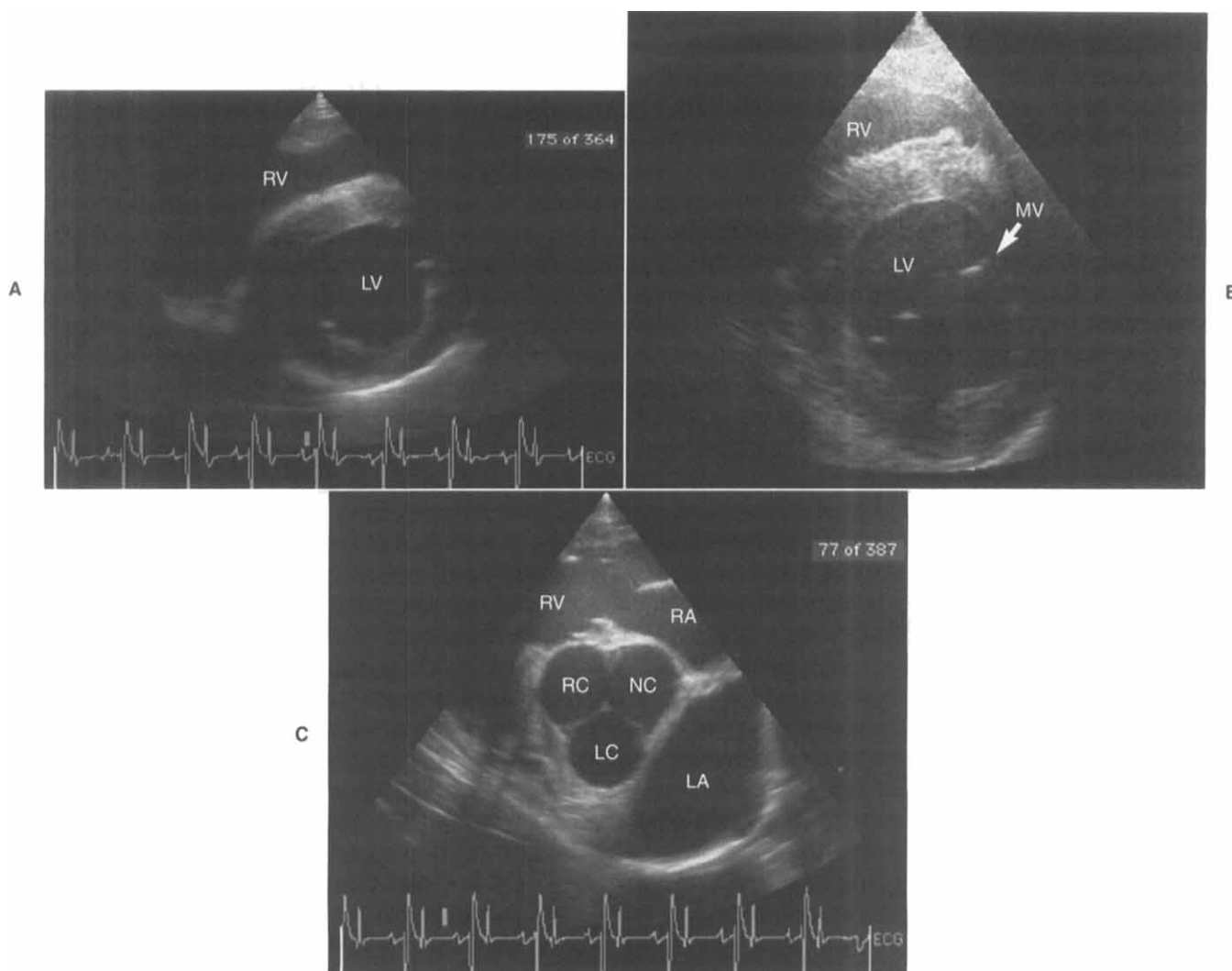


Figure 11.1-4 Standard short axis echocardiograms from the right side. **A**, Right parasternal short-axis view of the left ventricle at the chordal level. This view is used for M-mode examinations and measurement of the interventricular septum (IVS), left ventricle (LV), and right ventricle (RV) in systole and diastole from either the M-mode (motion mode) or two-dimensional (2-D) image. The ultrasonographic structure of the myocardium and left ventricular wall motion also can be assessed. The examiner must ensure that the image is a true short-axis, that is, papillary muscles are balanced. The papillary muscle may impinge on the M-mode cursor, giving the impression of increased contractility of the posterior free wall of the ventricle. This will increase artifactually the calculated fractional shortening and decrease the dimension of the LV. Trabeculae from the right ventricle must not be included in measurements of the IVS or left ventricular mass. *LV*, Left ventricle; *RV*, right ventricle. **B**, Right parasternal short-axis view of the left ventricle at the mitral valve level. This view is used to observe the mitral valve structure and motion and to record an M-mode of the mitral valve. *MV*, Mitral valve; *RV*, right ventricle; *LV*, left ventricle. **C**, Right parasternal short-axis view at the aortic valve level. This view is important to assess aortic valve structure, to record an M-mode through the aortic valve, to identify a membranous VSD as septal dropout between the mitral and aortic valve level, to identify thickness and loss of systolic vibration of the valve leaflets by M-mode, and to measure the left atrium and LA/AO ratio. *RC*, Right coronary cusp; *LC*, left coronary cusp; *NC*, noncoronary cusp of the aortic valve; *LA*, left atrium; *RV*, right ventricle; *RA*, right atrium. (Courtesy Dr. Karen J. Blissitt, Midlothian, United Kingdom, and Dr. Lesley E. Young, Newmarket, United Kingdom.)

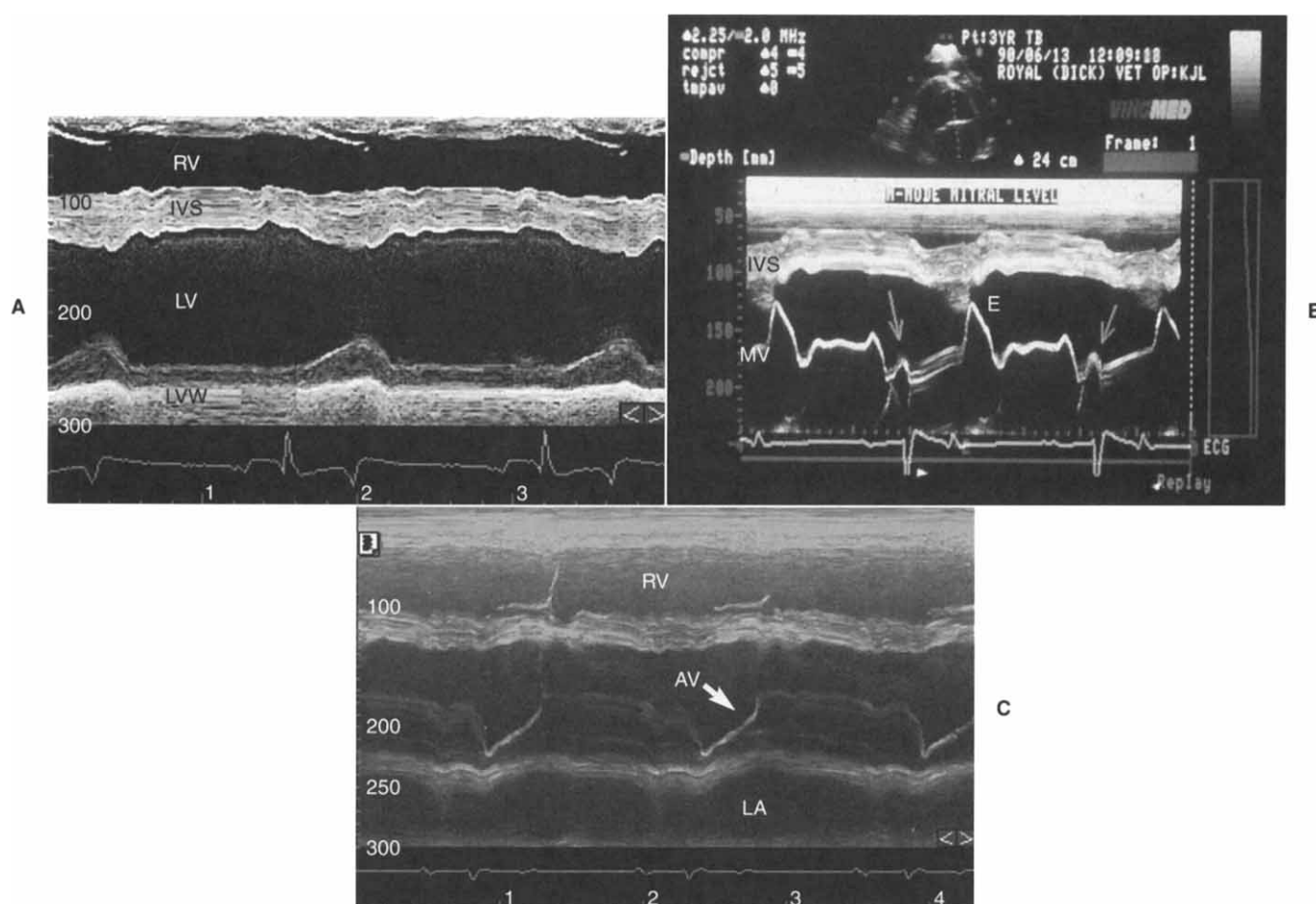


Figure 11.1-5 Standard M-mode echocardiograms. **A**, M-mode (motion mode) study recorded from a right parasternal short-axis view at the chordal level. By using short-axis images to guide placement of the M-mode cursor, the operator can ensure that the cursor is placed across the widest part of the chamber to be measured. The M-mode cursor is placed across the left ventricle (LV) so that the interventricular septum (IVS) and left ventricular wall are intersected at right angles. The following structures can be measured: left ventricular internal diameter in systole (LVIDs) and diastole (LVIDd), left ventricular wall in systole (LVWs) and diastole (LVWd), interventricular septum in systole (IVSs) and diastole (IVSd), and right ventricular internal diameter in systole (RVIDs) and diastole (RVIDd). From these measurements, the fractional shortening, a measure of contractility of the heart, can be calculated. **B**, M-mode study recorded from a right parasternal short-axis view at the mitral valve level. The M-mode cursor is positioned so that it bisects the left ventricle as described above. The opening of the mitral valve in early (E wave) and late (A wave) diastole can be seen. Note how the mitral valve leaflets start to open again after the A wave (arrows) as a result of the prolonged P-R interval. The distance between the point of maximal opening of the valve in early diastole (E point) and the IVS is a measure of dilatation of the left ventricle. The time and rate of opening and closure of the mitral valve can be measured, which provide information on the diastolic function of the ventricle. The M-mode view at this level also is used to observe vibrations of the mitral valve during diastole in cases of aortic insufficiency. **C**, M-mode study recorded from a right parasternal short-axis view at the aortic valve level. The cursor is positioned so that it bisects the aorta. The M-mode image is acceptable if one of the valve cusps can be seen during systole and diastole. The aortic diameter is measured using the leading edge method. This study is used to look at the normal movement of the aortic valve and aortic root. This image also can be used to measure ejection phase indices of ventricular function, the pre-ejection period and ejection time. RV, Right ventricle; AV, aortic valve; LA, left atrium. (Courtesy Dr. Karen J. Blissitt, Midlothian, United Kingdom, and Dr. Lesley E. Young, Newmarket, United Kingdom.)

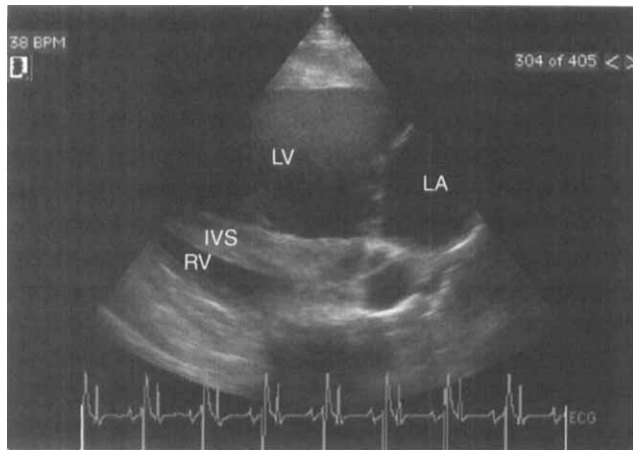


Figure 11.1-6 Parasternal long axis reference view of the left atrium and ventricle from the left hemithorax. This view is important to subjectively assess the mitral valve (thickness and motion), to evaluate the movement of the septum and free wall, to assess the relative size of the left atrium and ventricle, and to measure the left atrium (mitral annulus) and ventricle. Muscular ventricular septal defects may be visualized in this view. LV, Left ventricle; LA, left atrium; IVS, interventricular septum; RV, right ventricle. (Courtesy Dr. Karen J. Blissitt, Midlothian, United Kingdom, and Dr. Lesley E. Young, Newmarket, United Kingdom.)

the mitral and aortic valves for Doppler examination. The pulmonic valve and pulmonary artery are evaluated cranially, in the third intercostal space. Short axis views can be obtained by rotating the probe 90 degrees; if the entire heart does not fit on the screen from the right parasternal view, an M-mode of the left ventricle with calculation of FS can be obtained from the left parasternal short axis view. Table 11.1-1 gives normal ranges for selected cardiac M-mode and 2-D measurements.

Ancillary Tests

Laboratory Tests

Although biochemical analysis is usually not specific for cardiac disease, it is needed to assess the role of diseases of other body systems. In cases of arrhythmia, serum biochemical analysis of electrolytes, hepatic function, and renal indices are always necessary to rule out secondary myocardial involvement resulting from electrolyte disturbances, metabolic disease, or organ failure. Arterial blood gas values can be useful to determine the degree of venous admixture and the significance of complex congenital abnormalities because they provide an indication of both oxygenation and acid-base status. Venous blood gas and lactate analyses can be useful in a similar manner to monitor tissue perfusion and assess the severity of low-output failure.

Cardiac isoenzymes (cardiac troponin I [cTNI]; the cardiac isoenzyme of creatine kinase [CK-MB]; and the cardiac isoenzyme of LDH [HBDH]) are elevated in circumstances of myocardial inflammation, toxicosis, and necrosis. Similarly if the clinical history and echocardiography suggest an infective etiology, hematology and blood cultures are indicated. In cases of specific toxicosis (e.g.,

Table 11.1-1

Normal Ranges and Mean Values of Selected Cardiac Dimensions in Adult Horses

Cardiac Dimension	Min-Max (Mean)*	Min-Max (Mean)†
LVIDs (cm)	5.8-8.8 (7.45)	6.1-8.7 (7.35)
LVIDd (cm)	9.7-13.14 (11.92)	10.5-13.14 (11.90)
IVSs (cm)	3.16-5.16 (4.21)	3.3-5.6 (4.55)
IVSd (cm)	2.3-3.44 (2.85)	2.4-3.7 (3.02)
LVFWs (cm)	3.0-4.62 (3.85)	3.0-5.4 (3.96)
LVFWd (cm)	1.72-3.4 (2.32)	1.8-2.9 (2.39)
FS (%)	29.41-44.67 (37.42)	29-47 (38.76)
LAD (cm)	11.3-14.52 (12.82)	
Ao (cm)	6.9-9.22 (8.13)	7.7-9.5 (8.5)

LVID, Left ventricular internal diameter; *IVS*, interventricular septum; *LVFW*, left ventricular free wall; *s*, systole; *d*, diastole; *FS*, fractional shortening; *LAD*, left atrial diameter; *Ao*, aorta; *Min*, minimum value; *Max*, maximum value; *mean*, mean value.

Measurements are from M-modes (motion modes) of right parasternal short axis views, except LAD, which is from a left long axis two-dimensional (2-D) image.

*Data from Patterson MW, Gibbs C, Wotton PR et al: Echocardiographic measurements of cardiac dimensions and indices of cardiac function in normal adult Thoroughbred horses. *Equine Vet J Suppl* 1995; 19:18-27.

†Data from Long KJ, Bonagura JD Darke PGG: Standardized imaging technique for guided M-mode and Doppler echocardiography in the horse. *Equine Vet J* 1992; 24:226-235.

oleander or monensin exposure) appropriate toxicologic screening is recommended.

Radiography

Although thoracic radiography is commonly performed in horses, its sensitivity in diagnosing cardiac abnormalities is limited. Thoracic radiography is of greatest value to establish the presence of alveolar and interstitial edema secondary to congestive heart failure and to assess the pulmonary vasculature. Plain and contrast radiography has been replaced essentially by echocardiography for the diagnosis of structural cardiac abnormalities.

Cardiac Catheterization

This technique also has been superseded by the recent advances in noninvasive echocardiography. Cardiac catheterization now has little place in the diagnosis of cardiac disease in horses. Right heart catheterization is required for measurement of cardiac output by thermodilution, although the more recent modification of the dilution principle to use lithium means that cardiac catheterization for cardiac output estimation is also likely to become outmoded. Measurement of central hemodynamics for assessment of ventricular function, and hemodynamics using pressures derived from the cardiac chambers and great vessels are techniques that, although useful, are restricted to referral institutions and laboratories.

Supplemental Readings

- Blissitt KJ, Bonagura JD: Color flow Doppler echocardiography in normal horses. *Equine Vet J Suppl* 1995; 19:47-55.
- Blissitt KJ, Bonagura JD: Pulsed wave Doppler echocardiography in normal horses. *Equine Vet J Suppl* 1995; 19:38-46.
- Bonagura JD, Blissitt KJ: Echocardiography. *Equine Vet J Suppl* 1995; 19:5-17.
- Bonagura JD, Herring DL, Welker F: Echocardiography. *Vet Clin North Am Equine Pract* 1985; 1:311-333.
- Detweiler DK, Patterson DF: The cardiovascular system. In Catcott EJ, Smithcors JF (eds): *Equine Medicine and Surgery*, pp 277-347, Wheaton, Ill, American Veterinary Publications, 1972.
- Feigenbaum H: *Echocardiography*, 5th edition, Philadelphia, Lea & Febiger, 1994.
- Fregin GF: Cardiovascular sound and cardiac auscultation in the normal horse. *Comp Cont Educ (Suppl)* 1979; 1:S28-S32.
- Fregin GF: The equine electrocardiogram with standardized body and limb positions. *Cornell Vet* 1982; 72:304-324.
- Long KJ, Bonagura JD, Darke PGG: Standardized imaging technique for guided M-mode and Doppler echocardiography in the horse. *Equine Vet J* 1992; 24:226-235.
- Pipers FS, Hamlin RL: Echocardiography in the horse. *J Am Vet Med Assoc* 1977; 170:815-819.
- Reef VB: Evaluation of the equine cardiovascular system. *Vet Clin North Am Equine Pract* 1985; 1:275-288.
- Reef VB: Frequency of cardiac arrhythmias and their significance in normal horses. *Proceedings of the 7th American College of Veterinary Internal Medicine Forum*, pp 506-508, 1989.
- Reef VB: Heart murmurs in horses: determining their significance with echocardiography. *Equine Vet J Suppl* 1995; 19:71-80.
- Reef VB: Holter monitoring in the management of atrial fibrillation following conversion. *Proceedings of the 11th American College of Veterinary Internal Medicine Forum*, pp 610-613, 1993.
- Reef VB: Cardiovascular Ultrasonography. In Reef VB (ed): *Equine Diagnostic Ultrasound*, pp 215-225, Philadelphia, WB Saunders, 1998.

CHAPTER 11.2

Evaluation of Cardiovascular Function in the Performance Horse

MARY M. DURANDO
Davis, California

Cardiovascular abnormalities in resting horses are common. If the abnormalities are moderately severe they are fairly easily recognized. However, subtle or paroxysmal deficiencies in cardiovascular function also occur in horses that appear normal at rest but have a decrease in performance. These functional deficiencies may be easily overlooked, because many often only manifest during maximal exercise. This tendency is primarily due to the tremendous cardiovascular reserve of the horse, which is maximally used only during strenuous exercise. Conversely, physical examination may reveal moderately loud murmurs that, although readily apparent at rest, have no impact on performance. Horses have a high prevalence of both pathologic and physiologic arrhythmias and murmurs, and their significance is not always clear. Combined with the technical difficulties of the evaluation of myocardial function in exercising horses, these facts make it a challenge to determine the contribution of the cardiovascular system to performance problems of horses.

In essence, any condition that reduces a horse's cardiac output will reduce performance. Causes of poor perfor-

mance related to the heart include arrhythmias, systolic or diastolic dysfunction, valvular regurgitation, and intracardiac shunts. Severe regurgitation, large shunts, or sustained arrhythmias such as atrial fibrillation or ventricular tachycardia have an obvious impact on performance. However, because many of the abnormalities are paroxysmal or dynamic in nature (i.e., they occur only with exertion) an accurate diagnosis can be challenging. Therefore it is important to keep in mind that resting assessment of heart function may not correlate with function at high speed. To further complicate matters, abnormalities seen at rest may not affect performance at speed. Such conditions may simply disappear (e.g., arrhythmias) or have minimal negative impact (e.g., mild valvular regurgitation). For this reason, measurements made during exercise are more likely to correlate with exercising function than those made preexercise or postexercise. Many of the methods used to evaluate cardiac function in exercising horses are expensive, cumbersome, and only available at referral institutions. However, some of the simpler diagnostics, such as exercising telemetry, can be done in the field.

Supplemental Readings

- Blissitt KJ, Bonagura JD: Color flow Doppler echocardiography in normal horses. *Equine Vet J Suppl* 1995; 19:47-55.
- Blissitt KJ, Bonagura JD: Pulsed wave Doppler echocardiography in normal horses. *Equine Vet J Suppl* 1995; 19:38-46.
- Bonagura JD, Blissitt KJ: Echocardiography. *Equine Vet J Suppl* 1995; 19:5-17.
- Bonagura JD, Herring DL, Welker F: Echocardiography. *Vet Clin North Am Equine Pract* 1985; 1:311-333.
- Detweiler DK, Patterson DF: The cardiovascular system. In Catcott EJ, Smithcors JF (eds): *Equine Medicine and Surgery*, pp 277-347, Wheaton, Ill, American Veterinary Publications, 1972.
- Feigenbaum H: *Echocardiography*, 5th edition, Philadelphia, Lea & Febiger, 1994.
- Fregin GF: Cardiovascular sound and cardiac auscultation in the normal horse. *Comp Cont Educ (Suppl)* 1979; 1:S28-S32.
- Fregin GF: The equine electrocardiogram with standardized body and limb positions. *Cornell Vet* 1982; 72:304-324.
- Long KJ, Bonagura JD, Darke PGG: Standardized imaging technique for guided M-mode and Doppler echocardiography in the horse. *Equine Vet J* 1992; 24:226-235.
- Pipers FS, Hamlin RL: Echocardiography in the horse. *J Am Vet Med Assoc* 1977; 170:815-819.
- Reef VB: Evaluation of the equine cardiovascular system. *Vet Clin North Am Equine Pract* 1985; 1:275-288.
- Reef VB: Frequency of cardiac arrhythmias and their significance in normal horses. *Proceedings of the 7th American College of Veterinary Internal Medicine Forum*, pp 506-508, 1989.
- Reef VB: Heart murmurs in horses: determining their significance with echocardiography. *Equine Vet J Suppl* 1995; 19:71-80.
- Reef VB: Holter monitoring in the management of atrial fibrillation following conversion. *Proceedings of the 11th American College of Veterinary Internal Medicine Forum*, pp 610-613, 1993.
- Reef VB: Cardiovascular Ultrasonography. In Reef VB (ed): *Equine Diagnostic Ultrasound*, pp 215-225, Philadelphia, WB Saunders, 1998.

CHAPTER 11.2

Evaluation of Cardiovascular Function in the Performance Horse

MARY M. DURANDO
Davis, California

Cardiovascular abnormalities in resting horses are common. If the abnormalities are moderately severe they are fairly easily recognized. However, subtle or paroxysmal deficiencies in cardiovascular function also occur in horses that appear normal at rest but have a decrease in performance. These functional deficiencies may be easily overlooked, because many often only manifest during maximal exercise. This tendency is primarily due to the tremendous cardiovascular reserve of the horse, which is maximally used only during strenuous exercise. Conversely, physical examination may reveal moderately loud murmurs that, although readily apparent at rest, have no impact on performance. Horses have a high prevalence of both pathologic and physiologic arrhythmias and murmurs, and their significance is not always clear. Combined with the technical difficulties of the evaluation of myocardial function in exercising horses, these facts make it a challenge to determine the contribution of the cardiovascular system to performance problems of horses.

In essence, any condition that reduces a horse's cardiac output will reduce performance. Causes of poor perfor-

mance related to the heart include arrhythmias, systolic or diastolic dysfunction, valvular regurgitation, and intracardiac shunts. Severe regurgitation, large shunts, or sustained arrhythmias such as atrial fibrillation or ventricular tachycardia have an obvious impact on performance. However, because many of the abnormalities are paroxysmal or dynamic in nature (i.e., they occur only with exertion) an accurate diagnosis can be challenging. Therefore it is important to keep in mind that resting assessment of heart function may not correlate with function at high speed. To further complicate matters, abnormalities seen at rest may not affect performance at speed. Such conditions may simply disappear (e.g., arrhythmias) or have minimal negative impact (e.g., mild valvular regurgitation). For this reason, measurements made during exercise are more likely to correlate with exercising function than those made preexercise or postexercise. Many of the methods used to evaluate cardiac function in exercising horses are expensive, cumbersome, and only available at referral institutions. However, some of the simpler diagnostics, such as exercising telemetry, can be done in the field.

HISTORY AND PHYSICAL EXAMINATION

Many of the same historical questions detailed in the preceding Chapter 11.1 apply to the diagnosis of poor exercise performance. For instance, the clinician must ask questions that will help to identify either a gradual or an abrupt onset of clinical signs and their duration/progression. The clinician should also determine whether the horse ever performed well and if so, how long it has been performing poorly. Other helpful details about the decrease in the horse's performance include the point during a race when the horse slows down, how much its performance has deteriorated, and any other medical problems that may contribute to the decrease. A common complaint of owners is that a horse trains well and runs well during the initial portion of a race, only to fade in the last 2 or 3 furlongs. A thorough physical examination that includes careful auscultation, echocardiography, and electrocardiography should be completed before the exercising evaluation is performed. This procedure will rule out obvious resting abnormalities.

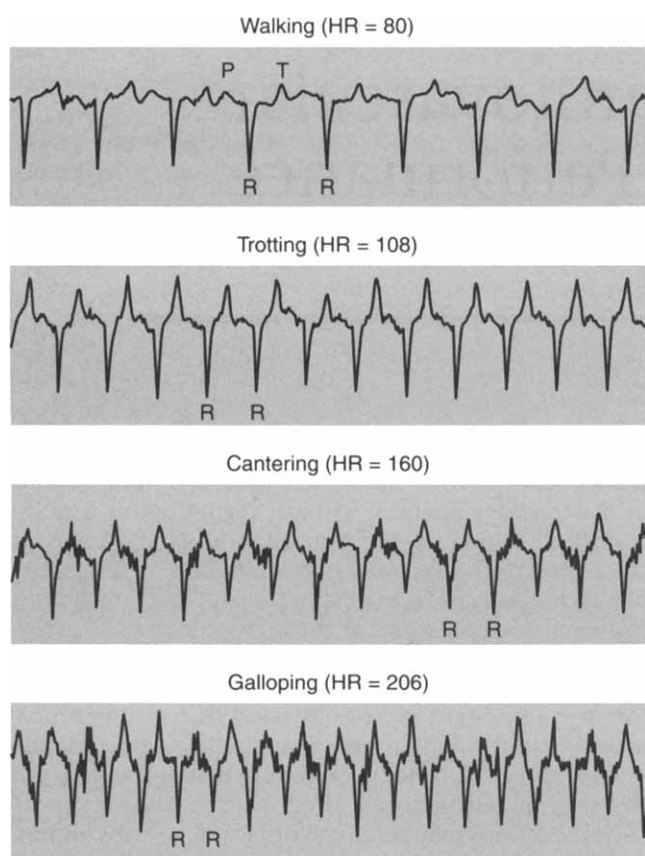


Figure 11.2-1 Base-apex electrocardiogram (ECG) recorded from a 4-year-old Thoroughbred exercising on a high-speed treadmill at different speeds. At the walk and trot the P waves are clearly distinct from the T waves; however, as the speed (and heart rate) increase the P waves become more difficult to distinguish. Although the depth of the R waves varies between beats, the configuration remains similar and the R-R interval remains regular.

STANDARDIZED EXERCISE TESTING

The most useful addition to the examination of horses for performance problems has been standardized exercise testing on a high-speed treadmill. This method has become an integral part of the complete examination and is essential for accurate diagnoses in elite athletic horses. Treadmill testing permits exercise in a controlled environment with reproducible conditions and circumvents many of the problems associated with attempts to acquire data from horses on a track. Diagnostic evaluations can be performed during and immediately after exercise while the horse is being monitored. The test can be tailored to the individual horse's ability, ranging from a slow gallop for those at risk for syncope and collapse to maximal speed for those in which it is important to mimic racing conditions. The test conditions also can be standardized to allow serial examinations to assess the effect of treatment. The vast majority of horses readily adapt to short-duration, high-intensity treadmill exercise, thus a standardized high-speed treadmill examination is most informative in the diagnosis of potential performance-limiting problems.

Heart Rate

Heart rate (HR) monitoring at specific exercise intensities and during the recovery period has been used to assess both fitness and cardiovascular disease. HR increases in response to exercise, with each gait having a fairly well-defined range. At a trot, HR is generally 80 to 120 beats per minute (bpm), 120 to 150 bpm while cantering, 150 to 180 at a gallop (not maximal effort) and as high as 240 bpm at maximal effort (Figure 11.2-1). Within 4 to 5 minutes after exercise the HR of healthy, well-conditioned horses should be less than 100 bpm. Horses with a HR greater than expected at a specific exercise intensity may have cardiac disease. However, HR may be increased above normal as the result of many other factors including lack of fitness, respiratory disease, musculoskeletal pain, or environmental factors such as heat and/or humidity. Therefore elevated HR is not pathognomonic for any specific disease process. Conflicting results on the effect of training on both exercising and postexercise heart rate exist in the literature. Heart rate may be influenced by temperature, humidity, and degree of fitness, as well as by cardiac disease. As with HR while exercising, a prolonged elevated postexercise HR may indicate cardiac disease, but other factors such as pain, environment, and respiratory disease must first be eliminated.

Electrocardiography during Exercise

The clinician's ability to diagnose cardiac dysrhythmias in exercising horses has been revolutionized by the development of systems capable of continuously monitoring the electrocardiogram (ECG). Although resting ECGs will show sustained arrhythmias such as atrial fibrillation or ventricular tachycardia that have an obvious negative impact on performance, a normal resting ECG does not preclude intermittent arrhythmias during exercise. Therefore heart rhythm is best examined under conditions that mimic a horse's required work level. This requirement can be best accomplished with telemetric ECG

or a continuous Holter monitor. Telemetry uses specially designed contact electrodes connected to a transmitting device. The contact electrodes, secured in place with a surcingle, are most commonly placed on the left, over the dorsal thorax (behind the withers), and at the cardiac apex. The transmitting device is attached to the surcingle near the withers and transmits the signal to a remote computer. Holter monitors have a similar set up except that the contact electrodes are connected to a recording device that directly records the heart rhythm, obviating the need for a distant receiver. The disadvantage of the Holter monitor is that the rhythm cannot be visualized until the recording is complete.

As mentioned previously, horses commonly have both physiologic and pathologic arrhythmias, and many times the significance of particular abnormal rhythms seen at rest is questionable. Because rhythm disturbances can be influenced by heart rate and changing vagal and sympathetic tone, it is critical to assess the effect of exercise on their occurrence. Many times resting arrhythmias, particularly those mediated by the vagus, may be abolished by exercise or events causing an increase in heart rate; these are considered unlikely to limit performance. Frequently, ar-

rhythmias can also be detected after exercise with auscultation. However, these are common findings in horses because of changing autonomic control, and are also usually insignificant. Conversely, horses with a normal resting rhythm may develop significant arrhythmias as they reach maximal speed or as they are finishing the test, which may be associated with slowing, weakness, collapse, or fatigue toward the end of a race (Figure 11.2-2). Continuous monitoring of the ECG during strenuous effort enables the clinician to characterize possible arrhythmias and when they occur in relation to exercise, to better assess their significance. The significance of an occasional isolated ectopic beat during exercise is more difficult to establish; however, it is possible that these could be exacerbated under racing conditions and cause decreases in athletic ability. In the immediate postexercise period, large fluctuations in autonomic tone occur. These fluctuations often result in transient arrhythmias that disappear when the heart rate returns to its resting rate. Sinus arrhythmias, second-degree atrioventricular block, and occasional isolated supraventricular and ventricular ectopic beats are considered clinically insignificant immediately postexercise. However, frequent ectopic beats, multiple pairs of ectopic beats, or

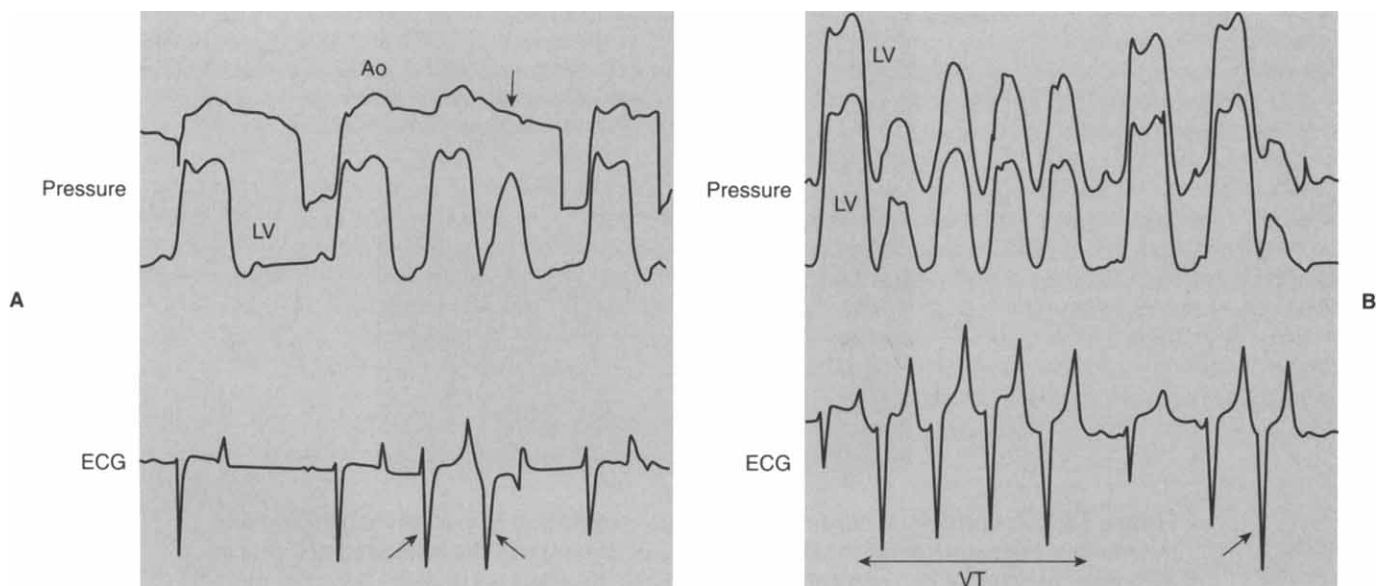


Figure 11.2-2 Electrocardiograms (ECGs) with concurrent pressure tracings show the effects of dysrhythmias on left ventricular (LV) and aortic pressure tracings. Note that in some cases the configuration of the QRS complexes of ectopic beats is clearly different, whereas in others the only way to identify the dysrhythmia is by the irregularity of the R-R interval. There is a clear effect of dysrhythmias on the pressure tracings, which shows that ectopic beats can have a negative impact on cardiac output in horses exercising at maximal intensity and thus may adversely affect performance. All ECG recordings were made with a base-apex lead system. Baselines have been shifted to permit visualization of the two pressure tracings. **A**, Recordings of 2 ventricular premature contractions from a standing horse (*lower panel, arrows*). Pressure transducers were placed in the left ventricle (LV) and aorta (Ao). Note the reduced LV pressure associated with the second premature beat. This reduced pressure is insufficient to open the aortic valve in systole and consequently there is no visible systolic pressure in the arterial pressure trace (pulse deficit; *upper panel, arrow*). **B**, A short run of ventricular tachycardia (VT) and an isolated ventricular premature contraction (*lower panel, arrow*) in a trotting horse. The LV pressures (*upper panel*) associated with the premature beats are significantly reduced compared with those from the sinus beats. Note there are two pressure transducers measuring LV pressure.

Continued

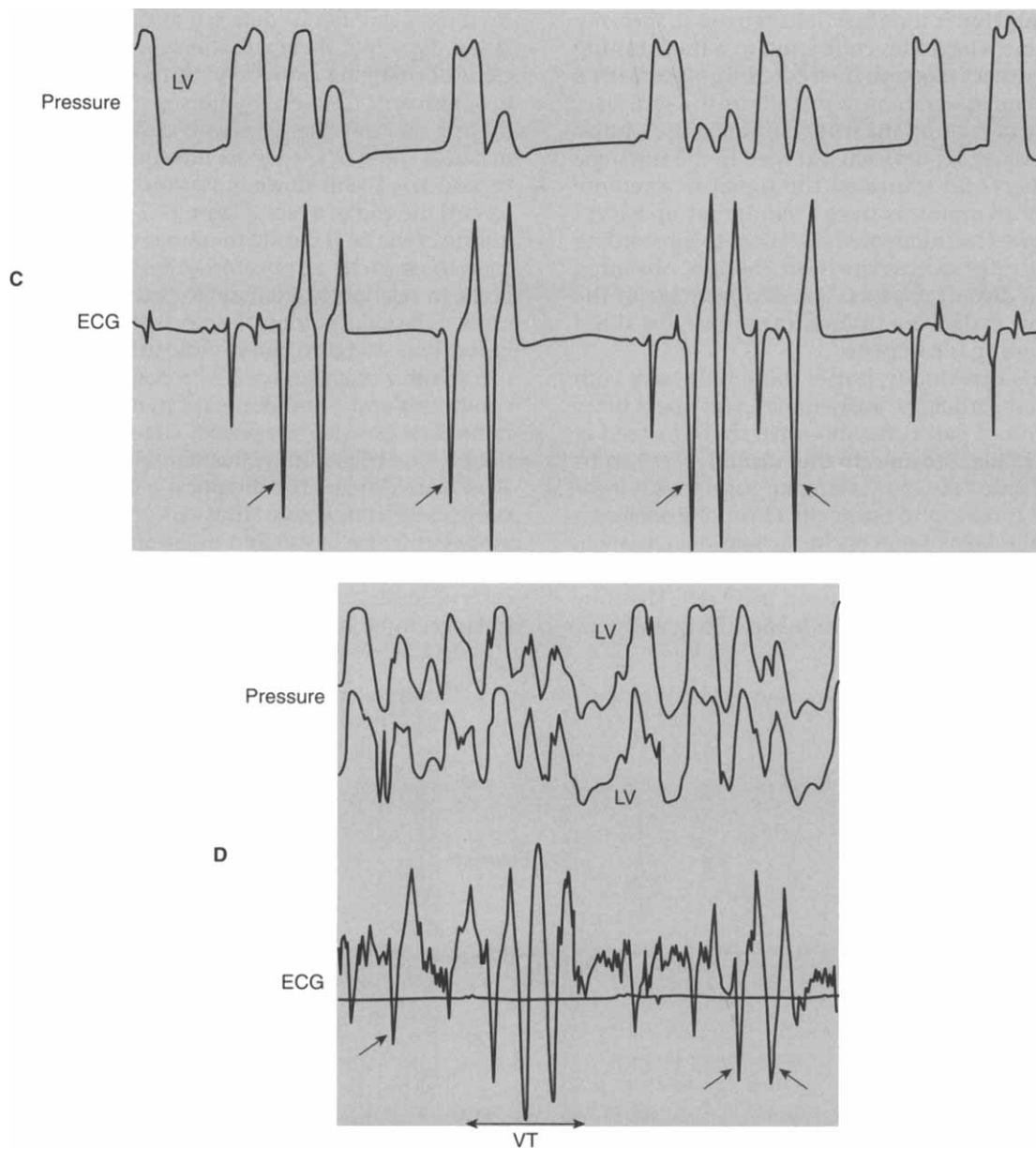


Figure 11.2-2, cont'd C, Ventricular premature depolarization in a standing horse. Note the multiple premature depolarizations (*lower panel, arrows*) and the associated decrease in LV systolic pressure. With consecutive ectopic beats, the effect on pressure becomes more profound. **D,** Multiple premature ventricular beats (*arrows*) and a short run of ventricular tachycardia (VT) in a galloping horse. Note the decrease in LV pressure (*upper panel*) caused by the dysrhythmias, particularly associated with the VT and the second of the two consecutive premature beats. Note there are two pressure transducers measuring LV pressure.

paroxysmal ventricular tachycardia are abnormal. The significance of these postexercise arrhythmias is not always clear, but their presence during maximal exercise helps to distinguish clinically significant arrhythmias.

Horses with clinically significant arrhythmias should have a thorough cardiac examination that includes an echocardiogram, 24-hour continuous ECG recording (Holter monitor), and measurement of serum electrolytes and cardiac isoenzymes. The latter include cardiac troponin-I (cTNI), and the myocardial isoenzyme of creatine

kinase (CK-MB). Because arrhythmias may be secondary to other disease states as well as primary in origin, the underlying cause should be determined, if possible. This determination may require evaluation of upper airway function by endoscopy and evaluation of pulmonary function by measurement of arterial blood gases during exercise. Identification of the underlying cause will help the clinician to institute appropriate management and treatment recommendations.

Abnormalities in the configuration of the ECG at rest

(particularly the T wave) have been examined to attempt to predict cardiac problems, however this has not proven to be a useful indicator. Training-induced changes in T-wave configuration in Thoroughbred and Standardbred racehorses have been shown. These changes are perhaps related to cardiac adaptation to training and resultant ventricular hypertrophy, as in human athletes.

ECHOCARDIOGRAPHY AFTER EXERCISE

Resting echocardiography clearly is the technique of choice to evaluate cardiac structure and function in detail in horses with overt or suspected cardiac disease. In the absence of clinically detectable cardiac disease, preexercise and postexercise echocardiography has also been used recently to evaluate horses with a history of exercise intolerance preexercise and post-exercise. Left ventricular dysfunction can manifest at rest without auscultatory abnormalities and is characterized by a decreased fractional shortening (FS), systolic ventricular wall thickening, and inward wall motion on the echocardiogram. Exercise intolerance has been attributed to myocardial dysfunction in horses with markedly decreased resting FS and wall motion that have no other obvious cardiac abnormalities. These horses are considered to have primary myocardial disease or cardiomyopathy. However, an abnormality during exercise could exist even with a normal echocardiographic examination at rest. During exercise, myocardial contractility increases, which is seen as an exaggerated wall motion and an increase in wall thickness and FS above resting values. These findings persist a brief time into the immediate post-exercise period, while the HR remains elevated, before returning to baseline values. Therefore, if these indices are evaluated immediately postexercise, they may give an indication of function during exercise. Exercise-induced myocardial dysfunction has been reported to occur in horses that appear to have a normal echocardiogram in a preexercise examination. In the postexercise examination, these horses show either no change or a decrease in FS, wall motion, and wall thickening over baseline measurements.

In humans, exercise stress echocardiography has been shown to be both a sensitive and specific indicator of coronary artery disease and myocardial ischemia. This method is as sensitive as coronary angiography in documenting exercise-induced ischemia and has the advantage of being noninvasive. To be most accurate, tests must be completed within 2 to 3 minutes after the end of exercise. After this time, values return to baseline in healthy human subjects. Therefore it is critical that the examination be completed quickly in humans; this also appears to be true in horses. Caution must be exercised in data interpretation if a delay in obtaining the images has occurred or the heart rate has decreased abruptly (as occurs in very fit horses or those not undergoing a sufficiently strenuous test), because these results may give a false impression of decreased wall thickening. Although arrhythmias, upper airway, and/or lower airway diseases have occasionally been seen in combination with myocardial dysfunction, often no other abnormalities are noted. The etiology for these findings in horses is not known, however, it may be associated with myocardial perfusion defects, exercising hypoxemia, myo-carditis, or myocardial dysfunction.

CARDIAC CATHETERIZATION

As previously mentioned, cardiac catheterization has largely been replaced by much less invasive imaging techniques that can provide estimates of myocardial function (e.g., Doppler echocardiography). However, under certain circumstances such as exercise, cardiac or pulmonary arterial catheterization can provide essential information regarding potential myocardial malfunction that cannot be obtained by any other method.

Although postexercise stress echocardiography can be used to provide some information regarding myocardial function during exercise, as discussed previously, technical and timing issues can lead to equivocal results. Additionally, mild cardiac dysfunction during exercise that may contribute significantly to decreased performance capabilities may not be detectable with current stress echocardiographic techniques. Advances in both human and equine cardiology have shown that mild myocardial abnormalities may be detected by using ventricular pressure dynamics in resting or anesthetized subjects. New technology has enabled accurate measurements to be made in maximally exercising horses, thus potentially allowing assessment of exercising function. Placement of catheters into the right ventricle is a relatively simple technique, although access to the left ventricle is usually not possible in a clinical situation and is presently only a research tool. To catheterize the right ventricle, a catheter introducer is placed into a jugular vein. A tip-mounted pressure transducer catheter is passed through the check-valve of the introducer and advanced to the ventricle. Correct placement is readily apparent from the form of the pressure signals as the catheter is advanced (Figures 11.2-3 and 11.2-4). In standing horses, flow-directed catheters are usually not required. It should be noted that placement of catheters into the ventricle is not without some risk. Although rarely persistent, arrhythmias associated with irritation of the myocardium can occur, as can thrombus formation and damage to valve leaflets and/or the myocardium. Studies conducted recently indicate slightly more arrhythmias during and following exercise with a right ventricular catheter than without, however, exercise with a right or a left ventricular catheter did not lead to increases in the circulating myocardial enzymes CK-MB or cTNI. Digital recording of ventricular pressures permits electronic/mathematical filtering of the data obtained during treadmill exercise to remove the effects of hoof impact on the pressure signals obtained (see Figure 11.2-4). Computations of rates and timings of these pressure changes during ventricular contraction/relaxation can provide valuable information regarding myocardial function. The effect that certain arrhythmias may have on ventricular function can also be clearly seen (see Figure 11.2-2). As collection of these types of data regarding cardiac function requires both a high-speed treadmill and pressure measurement/recording equipment, it is unlikely that such information can be obtained outside university hospitals or major referral centers. The readers are referred to the supplemental reading list for further details on these techniques.

An additional clinical use for cardiac catheterization would be to obtain estimates of cardiac output. Observed changes in cardiac output during anesthesia or drug therapy can be useful indicators of general cardiac function. Various indicator-dilution techniques can be used to pro-

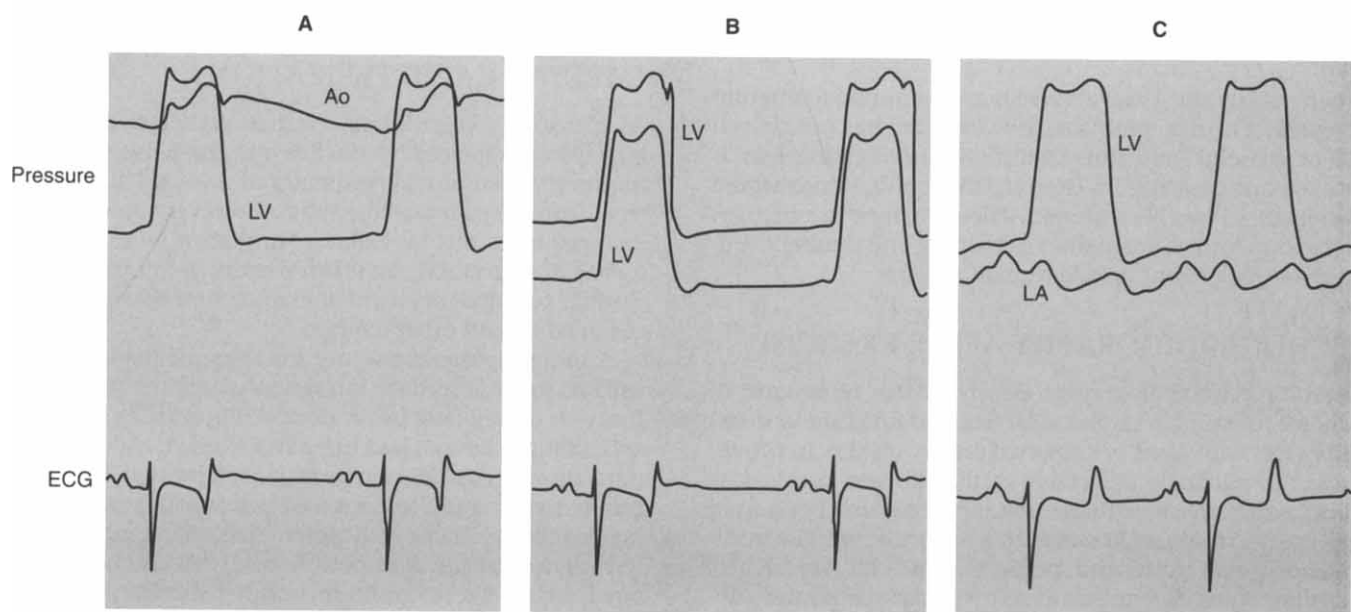


Figure 11.2-3 Pressure tracings of typical waveforms recorded from a dual-tipped, high-fidelity Millar catheter while it is passed through a carotid artery into the left ventricle and atrium. The corresponding electrocardiogram (ECG) is shown in the lower panel for timing of systole and diastole. **A**, The distal pressure transducer is in the left ventricle (LV) and the proximal transducer is in the aorta (Ao). **B**, Both the proximal and distal pressure transducers are in the LV. **C**, The distal sensor is in the left atrium (LA) and the proximal pressure transducer remains in the LV. Note the three pressure peaks associated with the left atrial sensor. The first peak is caused by atrial contraction and occurs after the P wave, the second is coincident with ventricular contraction after the QRS wave and is caused by the A-V valves bulging back into the atrium in early ventricular systole. The third occurs during atrial filling.

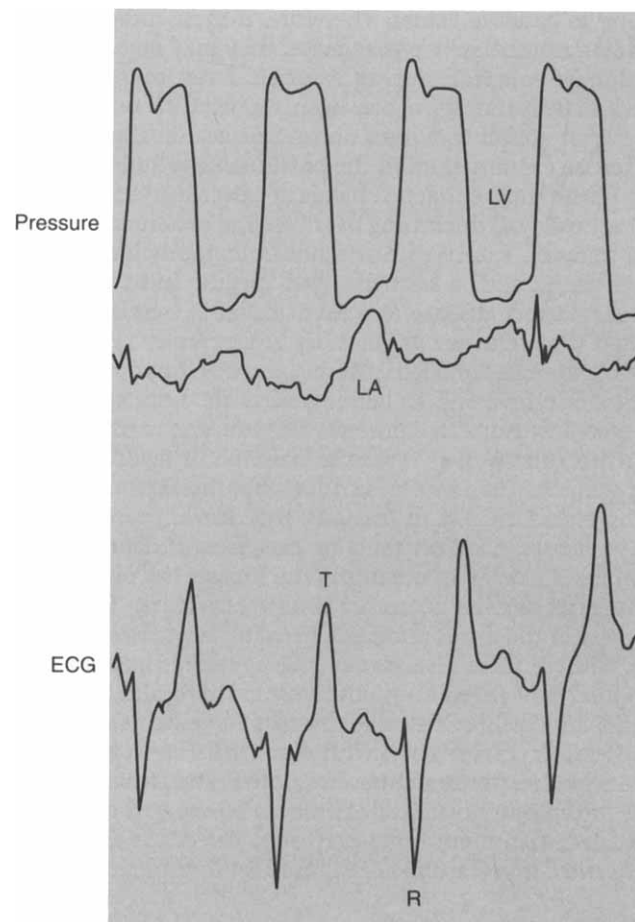


Figure 11.2-4 These recordings are made from a horse galloping with pressure transducers in the left atrium (LA) and left ventricle (LV). T and R waves of the ECG are indicated.

vide cardiac output estimates in resting or anesthetized horses, with thermodilution presently the most common. However, such techniques are generally unsuccessful during exercise. The most common method of estimating cardiac output during exercise is the Fick principle. For this method, not only are pulmonary and systemic arterial catheters required, but also oxygen consumption must be determined. Because determination of oxygen consumption usually requires that the horse wear some sort of mask over its nose to collect gases exhaled from the lungs, this technique is rarely performed in a clinical setting. A recently developed indicator-dilution technique that uses lithium as the indicator substance has been shown to provide reliable cardiac output measurements in both human and equine medicine without the need for cardiac catheterization. Catheters need only be placed in a jugular vein and a systemic artery such as the transverse facial artery. Data obtained with this system during high-speed treadmill exercise are promising, yet more studies will need to be conducted to evaluate its clinical usefulness and accuracy.

Supplemental Readings

Bayly WM, Gabel AA, Barr SA: Cardiovascular effects of submaximal aerobic training on a treadmill in Standardbred horses, using a standardized exercise test. *Am J Vet Res* 1983; 44:544-553.

Berberich SN, Zager JRS, Plotnick GD et al: A practical approach to exercise echocardiography: immediate postexercise echocardiography. *J Am Coll Cardiol* 1984; 3:284-290.

Blissitt KJ, Young LE, Jones RS et al: Measurement of cardiac output in standing horses by Doppler echocardiography and thermodilution. *Equine Vet J* 1997; 29:18-25.

Durando MM, Reef VB, Kline K et al: Effect of cardiac catheterization on cTNI and CK-MB in exercising horses. *Proceedings of the 19th American College of Veterinary Internal Medicine*, p 887, 2001.

Holmes JR: Cardiac arrhythmias on the racecourse. In Gillespie JR, Robinson NE (eds): *Equine Exercise Physiology 2*, pp 781-785, Davis, Calif, ICEEP Publications, 1987.

Linton RA, Young LE, Marlin DJ et al: Cardiac output measured by lithium dilution, thermodilution, and transesophageal Doppler echocardiography in anesthetized horses. *Am J Vet Res* 2000; 61:731-737.

Marr CM, Bright JM, Marlin DJ et al: Pre- and postexercise echocardiography in horses performing treadmill exercise in cool and hot/humid conditions. *Equine Vet J Suppl* 1999; 30:131-136.

Reef VB, Maxon AD, Lewis M: Echocardiographic and ECG changes in horses following exercise. *Proceedings of the 12th Annual Forum of the American College of Veterinary Internal Medicine*, pp 256-258, 1994.

Reef VB: Stress echocardiography and its role in performance assessment. *Vet Clin North Am Equine Pract* 2001; 17:179-189.

Sampson SN, Tucker RL, Bayly WM: Relationship between $\text{VO}_{2\text{ max}}$, heart score and echocardiographic measurements obtained at rest and immediately following maximal exercise in Thoroughbred horses. *Equine Vet J Suppl* 1999; 30:190-194.

Senta T, Smetzer DL, Smith CR: Effects of exercise on certain electrocardiographic parameters and cardiac arrhythmias in the horse: a radiotelemetric study. *Cornell Vet* 1970; 60:552-569.

Weigle GE, Langsetmo I, Gallagher RR et al: Analysis of right ventricular function in the exercising horse: use of the Fourier Transform. *Equine Vet J* 2000; 32:101-108.

CHAPTER 11.3

Congenital Heart Disease

JOHN D. BONAGURA
Columbus, Ohio

The equine heart must develop from an embryonic tube to a four-chambered pump secured by four valves and partitioned to serve the high-resistance systemic and low-resistance pulmonary circulations. The embryogenesis of the heart is complicated and occasionally the processes controlling normal cardiac development fail. Horses with mild to moderate congenital heart disease (CHD) may tolerate the disease well, although reproductive value of the animal surely suffers. Regrettably, the management options for moderate to severe CHD in horses are severely limited because most congenital heart defects can be treated only by surgery and under the control of cardiopulmonary bypass. Currently, this approach is unrealistic. This chapter presents a framework for understanding CHD in horses and offers specific guidelines

for recognition and assessment of the most important cardiac malformations.

NORMAL CARDIAC DEVELOPMENT

The underlying genetic factors guiding normal development of the heart and those leading to cardiac malformation are understood incompletely. Cardiac morphogenesis is complicated, but it is helpful to understand elementary aspects of cardiac development, especially as these pertain to CHD. Among these fundamentals are the septation of the atria, the anatomic components forming the ventricular septum, the separation of the great vessels, and the normal fetal circulation.

The right and left atria are separated by incorporation of

vide cardiac output estimates in resting or anesthetized horses, with thermodilution presently the most common. However, such techniques are generally unsuccessful during exercise. The most common method of estimating cardiac output during exercise is the Fick principle. For this method, not only are pulmonary and systemic arterial catheters required, but also oxygen consumption must be determined. Because determination of oxygen consumption usually requires that the horse wear some sort of mask over its nose to collect gases exhaled from the lungs, this technique is rarely performed in a clinical setting. A recently developed indicator-dilution technique that uses lithium as the indicator substance has been shown to provide reliable cardiac output measurements in both human and equine medicine without the need for cardiac catheterization. Catheters need only be placed in a jugular vein and a systemic artery such as the transverse facial artery. Data obtained with this system during high-speed treadmill exercise are promising, yet more studies will need to be conducted to evaluate its clinical usefulness and accuracy.

Supplemental Readings

Bayly WM, Gabel AA, Barr SA: Cardiovascular effects of submaximal aerobic training on a treadmill in Standardbred horses, using a standardized exercise test. *Am J Vet Res* 1983; 44:544-553.

Berberich SN, Zager JRS, Plotnick GD et al: A practical approach to exercise echocardiography: immediate postexercise echocardiography. *J Am Coll Cardiol* 1984; 3:284-290.

Blissitt KJ, Young LE, Jones RS et al: Measurement of cardiac output in standing horses by Doppler echocardiography and thermodilution. *Equine Vet J* 1997; 29:18-25.

Durando MM, Reef VB, Kline K et al: Effect of cardiac catheterization on cTNI and CK-MB in exercising horses. *Proceedings of the 19th American College of Veterinary Internal Medicine*, p 887, 2001.

Holmes JR: Cardiac arrhythmias on the racecourse. In Gillespie JR, Robinson NE (eds): *Equine Exercise Physiology 2*, pp 781-785, Davis, Calif, ICEEP Publications, 1987.

Linton RA, Young LE, Marlin DJ et al: Cardiac output measured by lithium dilution, thermodilution, and transesophageal Doppler echocardiography in anesthetized horses. *Am J Vet Res* 2000; 61:731-737.

Marr CM, Bright JM, Marlin DJ et al: Pre- and postexercise echocardiography in horses performing treadmill exercise in cool and hot/humid conditions. *Equine Vet J Suppl* 1999; 30:131-136.

Reef VB, Maxon AD, Lewis M: Echocardiographic and ECG changes in horses following exercise. *Proceedings of the 12th Annual Forum of the American College of Veterinary Internal Medicine*, pp 256-258, 1994.

Reef VB: Stress echocardiography and its role in performance assessment. *Vet Clin North Am Equine Pract* 2001; 17:179-189.

Sampson SN, Tucker RL, Bayly WM: Relationship between $\text{VO}_{2\text{ max}}$, heart score and echocardiographic measurements obtained at rest and immediately following maximal exercise in Thoroughbred horses. *Equine Vet J Suppl* 1999; 30:190-194.

Senta T, Smetzer DL, Smith CR: Effects of exercise on certain electrocardiographic parameters and cardiac arrhythmias in the horse: a radiotelemetric study. *Cornell Vet* 1970; 60:552-569.

Weigle GE, Langsetmo I, Gallagher RR et al: Analysis of right ventricular function in the exercising horse: use of the Fourier Transform. *Equine Vet J* 2000; 32:101-108.

CHAPTER 11.3

Congenital Heart Disease

JOHN D. BONAGURA
Columbus, Ohio

The equine heart must develop from an embryonic tube to a four-chambered pump secured by four valves and partitioned to serve the high-resistance systemic and low-resistance pulmonary circulations. The embryogenesis of the heart is complicated and occasionally the processes controlling normal cardiac development fail. Horses with mild to moderate congenital heart disease (CHD) may tolerate the disease well, although reproductive value of the animal surely suffers. Regrettably, the management options for moderate to severe CHD in horses are severely limited because most congenital heart defects can be treated only by surgery and under the control of cardiopulmonary bypass. Currently, this approach is unrealistic. This chapter presents a framework for understanding CHD in horses and offers specific guidelines

for recognition and assessment of the most important cardiac malformations.

NORMAL CARDIAC DEVELOPMENT

The underlying genetic factors guiding normal development of the heart and those leading to cardiac malformation are understood incompletely. Cardiac morphogenesis is complicated, but it is helpful to understand elementary aspects of cardiac development, especially as these pertain to CHD. Among these fundamentals are the septation of the atria, the anatomic components forming the ventricular septum, the separation of the great vessels, and the normal fetal circulation.

The right and left atria are separated by incorporation of

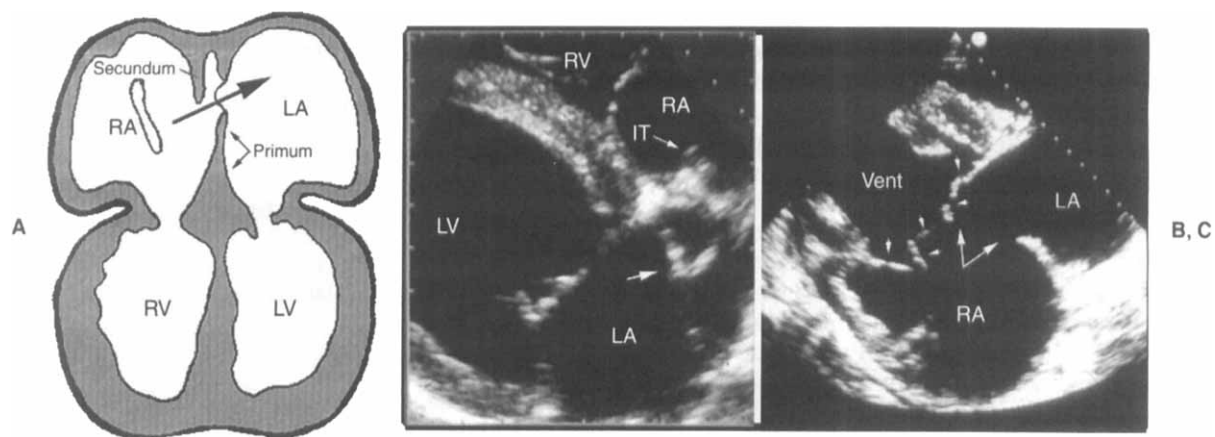


Figure 11.3-1 Atrial septal defects. **A**, This drawing demonstrates the tissues responsible for closing the atrial septum and the potential locations of atrial septal defects. The ventral atrial septum is closed by septum primum and the endocardial cushions. The dorsal atrial septum is formed by fusion of the septum secundum and the dorsal remnant of septum primum. The foramen ovale (*large arrow*) is a path for right to left shunting at the atrial level; a thin portion of septum primum forms the flap valve of this communication. The foramen ovale may persist in disorders characterized by elevated right atrial pressures. **B**, Two-dimensional echocardiogram obtained from a full-term foal showing the mobile membrane of the foramen ovale (*arrow*) pointed towards the left atrium. This is a normal finding. **C**, Endocardial cushion defect in a foal showing a large primum atrial septal defect (*arrows*) and a malformed, common atrioventricular valve (*double arrow*) guarding a large ventricle (uni-ventricular heart syndrome). The dorsal atrial septum (secundum) is evident between the left atrium and the dilated right atrium. RA, Right atrium; RV, right ventricle; LA, left atrium; LV, left ventricle; IT, intervenous tubercle; Vent, ventricle. (**A**, Courtesy Debra A. Primovic, DVM.)

the right horn of the sinus venosus and through development and fusion of two prominent membranes—septum primum and septum secundum (Figure 11.3-1). The endocardial cushions close the gap between the atrial and ventricular septa. These tissues also contribute to the atrioventricular septum, that segment filling the gap between the mitral valve septal insertion on the left and the more ventral tricuspid valve insertion on the right. The foramen ovale, a normal atrial structure, is located approximately in the middle of the atrial septum and creates a passageway for blood to flow from right to left atrium in the normal fetus. The equine foramen ovale resembles a fenestrated finger cot and can be observed echocardiographically as a mobile septal membrane even in healthy, full-term foals (see Figure 11.3-1). This inter-atrial path may persist in foals with pulmonary hypertension and elevated right atrial pressures. Failure of normal development in any of these tissues can lead to an atrial septal defect (ASD), which is typically designated by the location of the defective membrane.

The ventricular septum is a complicated partition that includes a small membranous portion located opposite the aortic root and craniodorsal to the tricuspid valve, an “inlet” septum below the septal tricuspid leaflet, an apically located muscular or trabecular septum, and a dorsal outflow segment that separates the subaortic and the subpulmonic infundibulum (Figure 11.3-2). The ventral atrial septum connects to the dorsal ventricular septum by growth and differentiation of endocardial cushions. These swellings also form the atrioventricular valves. Insufficient development of any embryonic component of

the ventricular septum can lead to a ventricular septal defect (VSD), the most common cardiac malformation in horses. Defective differentiation of the endocardial cushions causes various combinations of an ostium primum (ventral) ASD, an inlet VSD, malformation of the atrioventricular valves, or common atrium with a single atrioventricular valve.

The aorta and pulmonary artery begin as a single vessel in the conus arteriosus. This common vessel, the truncus arteriosus, eventually is partitioned by migration of the conus and development of the conotruncal and spiral septa. Twisting of the spiral septum produces appropriate alignment (concordance) of the great vessels with their respective ventricular chambers. The descending aorta and pulmonary artery are connected by the ductus arteriosus, which carries fetal blood from pulmonary artery to the descending aorta. Maldevelopment of conotruncal or spiral septal tissues leads to complicated congenital heart defects in the horse, including persistent truncus arteriosus and double outlet right ventricle. Persistent patency of the ductus arteriosus (PDA) is rare.

An understanding of the fundamental circulatory patterns of the fetus is helpful. Two circulations exist, one serving the embryo and the other communicating with the placenta. Functionally two right-to-left shunts exist: one across the foramen ovale and the other across the ductus arteriosus. The fetal lungs are collapsed, pulmonary vascular resistance is high, and pulmonary blood flow is minimal. Desaturated blood returning from the fetal tissues is collected in the cardinal venous system and enters

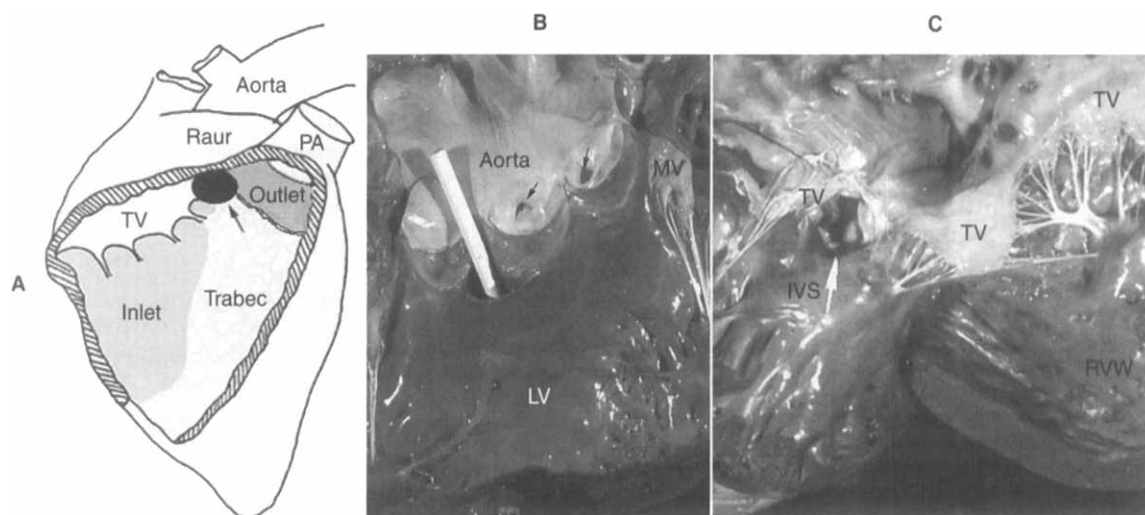


Figure 11.3-2 Ventricular septal defects. **A**, This drawing demonstrates components of the ventricular septum as viewed from the opened right ventricle and potential sites of ventricular septal defect (VSD). Shown are the membranous septum (*arrow*), inlet septum, trabecular septum (Trabec), and the outlet septum. **B**, Moderately-sized paramembranous VSD viewed from the left ventricular perspective. The defect is located adjacent to the noncoronary and right coronary cusps of the aortic valve (and is probed by a Bic ballpoint pen). Small arrows indicate the ostia of the right and left coronary arteries. **C**, Paramembranous VSD from another horse viewed from the right ventricular perspective. The septal tricuspid leaflet is retracted revealing the septal defect (*arrow*). The aortic valve is evident across the defect. The three leaflets of the tricuspid valve (TV) are labeled. IVS, Ventricular septum; RVW, right ventricular free-wall; Raur, right auricle; PA, pulmonary artery; MV, anterior mitral valve leaflet; LV, left ventricle. (Courtesy Debra A. Primovic, DVM.)

the sinus venosus and right atrium. This blood is earmarked primarily for the right ventricle and pulmonary artery. Most pulmonary arterial flow is diverted through the ductus arteriosus to the descending aorta and placenta where it is oxygenated. Well-saturated blood returning across the umbilical veins is delivered by the caudal vena cava to the right atrium where it preferentially crosses the foramen ovale to enter the left atrium, left ventricle, and ascending aorta.

These patterns change dramatically with foaling. As the lungs expand, pulmonary vascular resistance falls, and pulmonary blood flow increases. The resultant increase in left atrial pressure functionally closes the foramen ovale within the first 24 to 48 hours of life. Similarly, inhibition of local prostaglandins leads to functional closure of the ductus arteriosus within 72 hours in most full-term foals. Persistence of the right-to-left shunts, especially at the level of the foramen ovale, can occur in premature foals or those suffering from severe pulmonary disease with associated pulmonary hypertension. In these cases, shunting across the foramen ovale represents an additional mechanism for arterial desaturation and tissue hypoxia.

ETIOLOGY AND PREVALENCE OF CONGENITAL HEART DISEASE

A failure of normal fetal development may result in congenital malformation of the heart, great vessels, or veins. The etiology of CHD in most cases is uncertain and may be

related to genetic liability or defective genetic control, fetal infection, drug administration to the mare, or fetal exposure to toxins *in utero*. Dogs have clear breed associations to CHD, but scant information is available about the heritable nature of CHD in horses. Arabian horses are apparently at risk for ventricular septal defects and conotruncal septal defects. However, no comprehensive surveys of equine breeds associated with cardiovascular malformations have been published.

The exact prevalence of CHD in the general equine population is unknown, but cardiac malformations were reported in 3.5% of 608 foals examined at necropsy. Theoretically, a great number of cardiac malformations could occur, including anomalies of the following:

1. Venous drainage
2. Atrial situs or septation
3. Atrioventricular connection
4. Ventricular development (including formation of the two atrioventricular valves)
5. Ventricular outflow tracts
6. Semilunar valves
7. Great vessels

Furthermore, abnormal segmental connections might occur leading to "discordance" in the path of systemic or pulmonary venous return relative to the pulmonary artery or aorta. These abnormalities include transposition of the great vessels and double-outlet ventricle, wherein both great vessels exit the right or left ventricular cavity.

However, practically speaking, the most common cardiac malformations in horses involve shunting of blood at the atrial or ventricular levels.

Thus the horse with CHD most often presents with findings related to a VSD. The isolated VSD adjacent to the membranous septum represents the most common malformation, although VSD involving the trabecular septum, atrioventricular septum, or the outflow septum also have been recognized. Ventricular septal defect is a component of tetralogy of Fallot, persistent truncus arteriosus, and most cases of pulmonary and tricuspid valve atresia. Most rare forms of equine CHD such as tricuspid valve atresia, double-outlet ventricle, transposition of the great vessels, and univentricular heart syndromes also usually are associated with a VSD. The isolated ASD is rare in horses, but secundum defects, primum defects, and common atrioventricular canal defects have been observed. Patent ductus arteriosus as a single defect is rare in horses; however, a PDA may accompany other defects, including pulmonary atresia. Equine CHD characterized by primary valvular disease is exceedingly rare, although tricuspid atresia, bicuspid (stenotic) pulmonary valve, and fenestrated aortic valve have been observed. Other rare malformations in Equidae include hypoplastic left heart syndrome, single ventricle/univentricular heart complexes, endocardial fibroelastosis, aortic origin of the pulmonary artery, various coronary artery anomalies, and interruption of the aortic arch.

CLINICAL PATHOPHYSIOLOGY OF SHUNTS

Fundamental to understanding cardiac malformations in the horse are appreciation of shunt physiology and the potential responses of the heart and circulation to a shunt. Shunting can be defined as abnormal deviation of blood flow between the systemic (left) and pulmonary (right) sides of the circulation. Possibilities include left-to-right, right-to-left, and bidirectional shunting.

Systemic to pulmonary (left-to-right) shunting is the expected consequence of an ASD, VSD, or PDA so long as systemic pressures and resistances exceed those on the right side. Even in cases of abnormal ventricular-arterial development, as with persistent truncus arteriosus, double outlet right ventricle, or univentricular heart, the clinical findings of a left-to-right shunt may predominate unless obstruction to blood flow occurs at the pulmonary valvular or arteriolar levels. The actual shunt volume carried to the lungs depends on the caliber (or "restrictive" nature) of the lesion orifice and the relative resistances between the systemic and pulmonary circulations. Shunting may not be significant after foaling because pulmonary vascular resistance is still relatively high and systemic arterial and left ventricular pressures are relatively low for a number of weeks after birth. Eventually left-to-right shunts increase pulmonary arterial flow and augment pulmonary venous return. Small shunts are handled easily through mild left-sided dilation and hypertrophy. When the pulmonary to systemic flow ratio ($Q_p:Q_s$) exceeds about 1.8:1, the shunt usually is considered clinically significant. The result is more noticeable volume overload of the left atrium and left ventricle. The greater the shunt, the higher the potential for left-sided or biventricular congestive heart failure (CHF) from chronic ventricular systolic or diastolic dys-

function (Figure 11.3-3). Pulmonary hypertension can occur in the setting of left-to-right shunting from combinations of increased flow, inadequate development of pulmonary arterioles, and left ventricular dysfunction. Thus, consequences of significant left-to-right shunting may include any of the following: exercise intolerance, tachypnea, pulmonary edema, respiratory distress, pulmonary hypertension, atrial fibrillation, pleural effusion, jugular venous distention, or ventral edema. The foal may be smaller than expected and may have a history of antibiotic therapy for presumed bouts of "pneumonia."

Right-to-left shunting stems from a different pathophysiologic state and produces another clinical presentation. When a shunt is complicated by a right-sided obstruction adjacent to or downstream from the defect, right-to-left shunting develops as right-sided pressures exceed those on the left side. This can occur in the neonate, as in tricuspid valve atresia with ASD or pulmonary valve atresia with VSD. Conversely, elevated right-sided resistance can develop more chronically from pulmonary vascular disease. For example, a large left-to-right shunt can induce medial hypertrophy and intimal thickening of pulmonary arterioles elevating pulmonary vascular resistance and decreasing the left-to-right shunt (see Figure 11.3-3). Although uncommon, the resultant pulmonary hypertension may become quite severe (Eisenmenger's physiology) and reverse the shunt to right-to-left. In these cases the left heart chambers are small and right ventricle is hypertrophied to achieve systemic blood pressure.

The entrance of desaturated blood from the right to left side of the circulation causes hypoxemia. Thus the consequences of a significant right-to-left shunt may include low arterial PO_2 , tissue hypoxia, cyanosis, exercise intolerance, mild to moderate polycythemia, hyperviscosity of blood, and stunting of growth. Congestive heart failure is rare, but sudden death can occur, presumably from arrhythmia. The degree of hypoxemia and cyanosis in a right-to-left shunt depend on overall pulmonary blood flow; this is a pivotal concept. If pulmonary flow is diminished, as with tetralogy of Fallot, tricuspid atresia, and pulmonary atresia with VSD, the contribution of the left ventricle to aortic flow (and thus oxygenation) is low.

In some instances right-to-left shunting develops in the setting of increased pulmonary blood flow, as with truncus arteriosus or double outlet ventricle. These lesions cause less hypoxemia because the amount of oxygenated blood reaching the left ventricle is normal to increased. In such situations cyanosis from right-to-left shunting may be negligible and the clinical condition of left sided or biventricular congestive heart failure may predominate. If the increased pulmonary flow is sufficient to minimize the arterial hypoxemia but not cause CHF, survival beyond 5 years of age is possible.

CLINICAL SIGNS AND DIAGNOSTIC APPROACH

Although CHD is relatively uncommon in Equidae, a diagnosis of cardiovascular malformation can affect significantly the value of the foal and cast doubt on the genetic reliability of the mare or sire. The clinical impact of a congenital heart defect in an individual horse can vary widely.

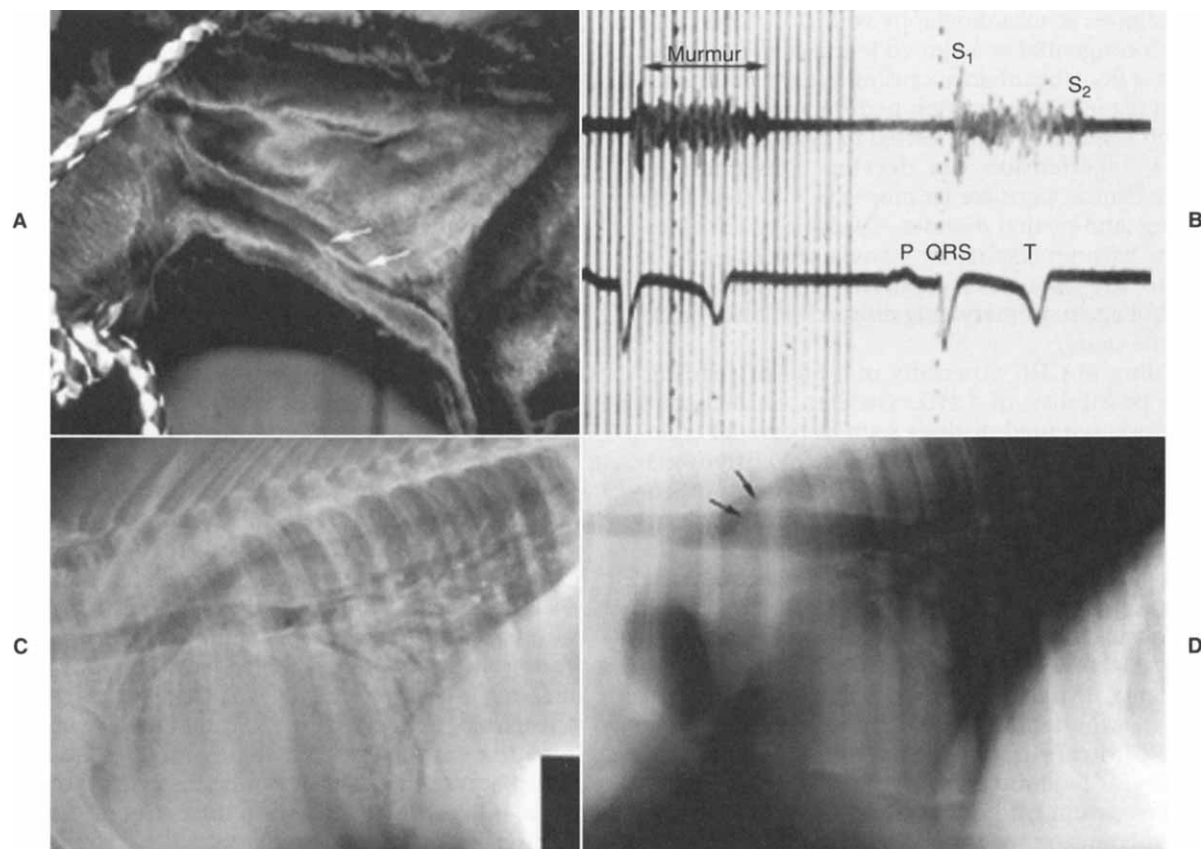


Figure 11.3-3 Clinical findings in congenital heart disease. **A**, Jugular venous distention (arrows) in a foal with congestive heart failure (CHF) caused by congenital heart disease. **B**, Holosystolic murmur recorded from a foal with a ventricular septal defect. The first and second heart sounds also are labeled. P-QRS-T refers to waves of the accompanying electrocardiogram. **C**, Lateral radiograph from a horse with left-sided CHF resulting from a left to right shunt. Note the increase in heart size and prominent pulmonary vascularity. The pulmonary infiltrates are compatible with edema. **D**, Lateral radiograph from a foal with cyanotic congenital heart disease and a right-to-left shunt. The overall heart size is not greatly enlarged, but a prominence in the aortic arch is related to dilation of this vessel. Pulmonary vascularity is reduced markedly.

Some malformations are lethal *in utero* or immediately after parturition; whereas, others cause signs only later in life. Other defects are compatible with a near-normal life expectancy but limit maximum performance and reproductive value. Mild or trivial defects do not affect performance and may escape detection.

The diagnosis of CHD in horses requires an index of suspicion because no clinical findings are specific for cardiac malformation. Certainly a cardiac murmur is the most common clinical finding in CHD, but other signs, such as reduced performance, tachypnea, respiratory distress, or cyanosis, may be observed in symptomatic animals. In some severe cases, atrial fibrillation or signs of congestive heart failure (CHF) are evident (see Figure 11.3-3).

The timing and location of a heart murmur associated with CHD varies with the defect (as discussed later). Ejection murmurs are ubiquitous in horses, and these can pose a diagnostic dilemma. An ejection murmur loudest over the left-cranial cardiac base may be evident with some car-

diac defects, but this murmur is even more common in foals and adults without heart disease. In most cases, a left basilar ejection murmur simply represents a functional (flow) disturbance unrelated to heart disease. The usual functional murmur builds in midsystole, ends before the second sound, and varies in intensity with sympathetic activity. Ejection murmurs usually become louder briefly after exercise or after a startle reaction. Echocardiography and Doppler studies should be normal in the horse with a functional murmur. Conversely, a cardiac murmur with one or more of the following characteristics is more likely to be associated with structural heart disease:

1. Moderately loud (>3/6) murmur
2. Precordial thrill
3. Holo- or pansystolic in timing
4. Diastolic or continuous in timing
5. Loudest over the palpable left apex or over the right side of the thorax

In these instances echocardiography with Doppler is likely to identify a congenital or acquired lesion of the heart, or at the least, a flow disturbance causing the murmur (such as tricuspid regurgitation in high-performance horses).

Although respiratory signs related to heart failure or to pulmonary hypertension can develop consequent to CHD, these clinical signs are far more likely to stem from airway, lung, and pleural diseases. Cyanosis in a foal, especially one without respiratory distress, should alert the clinician to the possibility of CHD with right-to-left shunting; but again, primary lung disease first must be excluded as the cause.

The finding of CHF, especially in a foal or yearling, raises the possibility of CHD. Differential diagnosis should include acquired diseases such as bacterial endocarditis, pericarditis, myocarditis, and tachyarrhythmia-induced cardiomyopathy (from relentless supraventricular or ventricular tachycardia). Infrequently, CHD leads to heart failure in a mature horse, and in these cases, the diagnosis is usually accidental, made during echocardiographic examination. Right-sided CHF is a straightforward diagnosis characterized by resting tachycardia, bilateral jugular venous distention, jugular pulses, and ventral edema. If pulmonary hypertension occurs the pulmonic component of the second sound may be tympanic. Clinical findings of left-sided CHF include resting tachycardia, loud third heart sound, and auscultatory or percussion findings of pulmonary edema, pulmonary hypertension, or pleural effusion. Atrial fibrillation and cardiac murmurs are other common findings. Biventricular CHF is not uncommon in horses with cardiac failure and is most often observed with the combination of a left heart lesion, pulmonary hypertension, and atrial fibrillation.

The most important diagnostic studies in foals with suspected CHD include the following:

1. Palpation of the arterial pulse for rate, rhythm, and strength
2. Examination of the precordium for thrills or cardiac displacement
3. Careful auscultation of the heart, lungs, and pleural space
4. Inspection of mucous membranes
5. Assessment of the jugular venous pulse and pressure
6. Thoracic radiography, thoracic ultrasonography, or airway endoscopy/cytology when signs of lung or pleural disease are present
7. Echocardiography complemented by Doppler studies

The latter examination represents the noninvasive gold standard for diagnosis of CHD. Should a cardiac malformation be found in a foal, the clinician should at least auscultate the mare for evidence of CHD.

VENTRICULAR SEPTAL DEFECT

Ventricular septal defect (VSD) is the most important CHD of horses. A genetic basis is likely in the Arabian breed. In this author's experience, VSD also is encountered regularly in Standardbred horses and in Quarterhorses. The VSD often accompanies more complicated malformations.

Pathology

The location of a VSD depends on the embryogenesis of the lesion (see Figure 11.3-2) and influences the designation and even the clinical manifestations of the defect. The nomenclature of VSDs is very confusing, but most can be remembered by considering the main components of the normal ventricular septum. In most cases, a VSD is located dorsally ("high") on the ventricular septum, below the right or noncoronary cusp of the aortic valve on the left side, and craniodorsal to the septal tricuspid leaflet on the right (Figure 11.3-4; see also Figures 11.3-2 and 11.3-3). Such defects are generally termed *perimembranous*, or perhaps more correctly, *paramembranous*. Most of these holes are also "subcrestal" because the VSD is located caudoventral to the muscular supraventricular crest that separates the right ventricular inlet and outlet. However, a very large paramembranous defect may extend under the tricuspid valve towards the inlet septum or advance across the supraventricular crest towards the outlet septum. The (conotruncal) septal defects associated with tetralogy of Fallot and with pulmonary atresia are usually very large, and fall into the latter appellation. Sometimes the aortic root is displaced ventrocranially and straddles the defect, creating a "malalignment" VSD. This is characteristic of the tetralogy of Fallot but also can be seen with large paramembranous defects. Malalignment is clinically significant because the right or noncoronary cusp of the aortic valve is likely to prolapse into the defect leading to aortic regurgitation.

A less common location for a VSD is immediately ventral to the septal tricuspid valve within the muscular septum. Such "inlet" VSDs are typical of an endocardial cushion defect and may be related to a primum ASD or even a persistent common atrioventricular canal, which creates a gap between all four cardiac chambers. A subaortic VSD that communicates with the outlet portion of the ventricular septum directly below the pulmonary valve is variably termed an "outlet," "supracristal," "subpulmonic," "subarterial," or "doubly-committed" VSD. This lesion also places the aortic valve at risk for prolapse. Apical muscular (trabecular) defects or multiple VSDs are rare but have been observed in horses. Some of these are small, although others have been enormous.

Many VSDs close spontaneously in people, but whether this is common in horses is unknown. However, the flow across a VSD can be diminished by imposition of a cardiac valve. For example the rim, or even a major portion of a VSD, may be occluded by scar tissue that ensnares the septal tricuspid leaflet, rendering the defect functionally smaller and possibly creating a hyperechoic aneurysm on the right septal surface. Large defects associated with malalignment of the ascending aorta to the upper border of the remaining septum often are associated with prolapse of an aortic valve leaflet (or of the aortic root) into the defect. Aortic prolapse can close even a large VSD effectively but at the risk of permitting chronic aortic valve insufficiency over time.

Pathophysiology and Clinical Signs

The pathophysiology of the uncomplicated VSD is that of a left-to-right shunt as described previously. Much of the

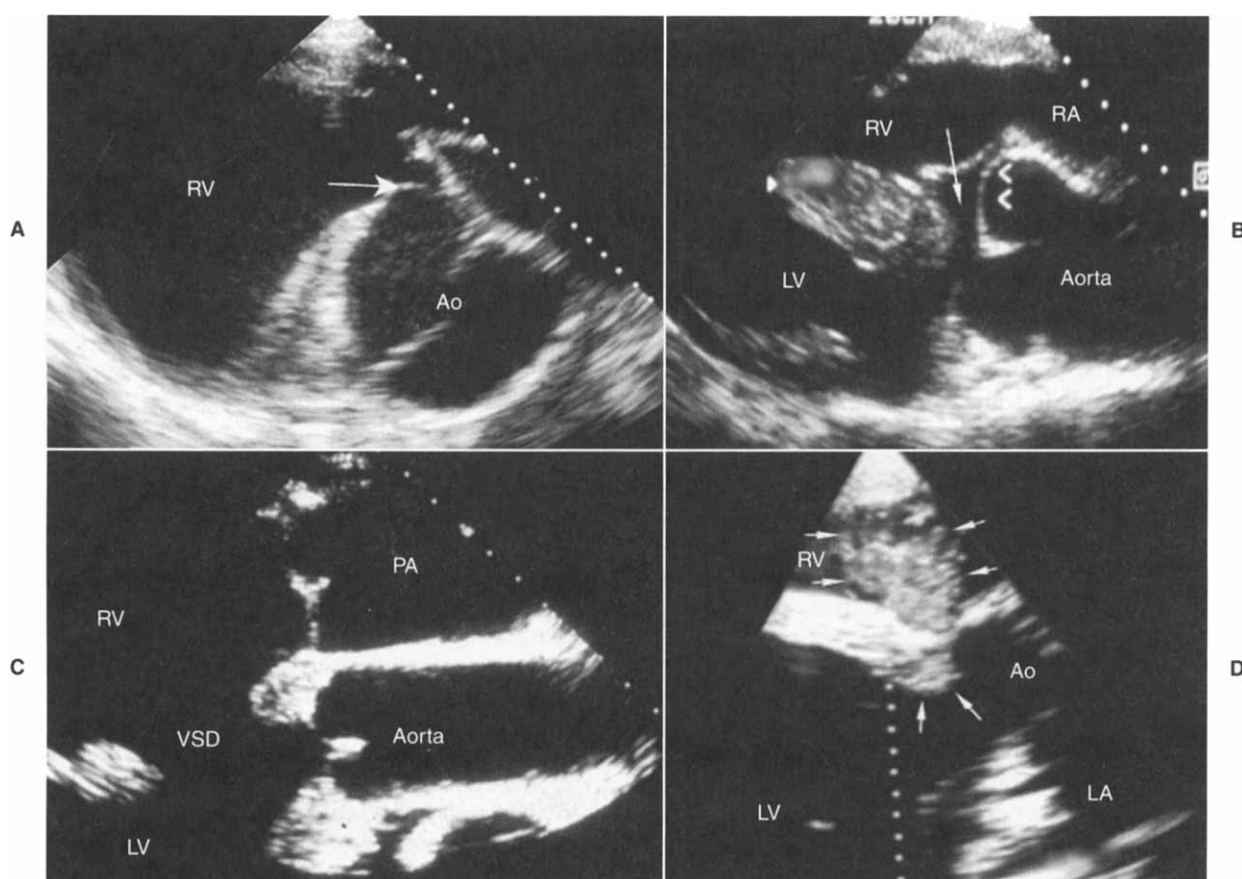


Figure 11.3-4 Ventricular septal defects (VSDs): echocardiography. **A**, Regionally enhanced image of the aortic root demonstrating a small paramembranous VSD entering below the septal tricuspid leaflet. The aortic root is also dilated and the aortic valve leaflets are unequal suggesting root prolapse or aortic valve malformation. **B**, Malalignment paramembranous VSD in an Arabian horse with marked overriding of the aortic root and prolapse of an aortic valve into the defect (*arrowheads*). A small communication is still evident between the ventricles (*arrow*). **C**, Regionally enhanced view of a large subarterial VSD in a horse with malpositioned great vessels. Functionally there is a left to right shunt as evident by the marked dilation in the pulmonary artery (PA). A portion of the infundibular septum can be seen at the lower left, under the VSD. **D**, Black-and-white image of a color-Doppler echocardiogram obtained from a horse with a typical paramembranous VSD. Flow from the left to right shunt is outlined (*arrows*). The defect itself is not readily seen. Ao, Aorta; RV, right ventricle; LV, left ventricle; RA, right atrium; LA, left atrium.

shunt volume pumped by the left ventricle is ejected immediately into the pulmonary artery. As pulmonary flow increases, increased venous return occurs to the left atrium and left ventricle, causing left ventricular dilation and hypertrophy that can be recognized by echocardiography. Thus the left (not the right) ventricle performs most of the extra volume work. This is made more severe in cases of aortic valve prolapse with aortic regurgitation or if mitral regurgitation develops owing to left ventricular enlargement. If the shunt is large and pulmonary arteriolar resistance does not increase significantly, left ventricular failure can develop. This is most likely to occur early in life as the high fetal pulmonary vascular resistance declines, but late cases of CHF (with atrial fibrillation) also have been observed. The degree of RV hypertrophy and enlargement varies, depending on the location and size of the septal

defect and pulmonary vascular resistance. Large nonrestrictive defects cause the two ventricles to behave as a common chamber, allowing ventricular pressures to equilibrate, and leading to severe RV hypertrophy in addition to pulmonary hypertension.

The clinical features of VSD are variable. Clinical signs may be absent and the defect identified as an incidental finding. A mature horse may be presented for poor performance or with atrial fibrillation. Foals may be symptomatic for pulmonary edema or biventricular heart failure. Most commonly, the clinician detects a murmur incidentally during the physical examination for another problem or during a prepurchase examination (see Figure 11.3-3). Because most defects communicate near the RV inlet septum, the most consistent physical examination finding is a harsh, holosystolic, or pansystolic murmur that is loudest

just below the tricuspid valve and above the right sternal border. An ejection murmur (one to two grades softer) of relative pulmonic stenosis (from increased flow) is usually evident over the left base. The second heart sound may be split more widely than normal because of disparate ventricular ejection times; the pulmonic component of S_2 may be more tympanic if there is pulmonary hypertension.

In contrast the murmur of a subarterial (subpulmonic or supracristal) VSD is loudest over the left cranial base as the high velocity flow enters just below the pulmonary artery. When VSD is associated with complex cardiac malformation, the murmur is likely to be loud over each side of the thorax. The severity of the defect cannot be judged based on murmur intensity. In some cases, a small defect may be quite loud, whereas a large, less restrictive defect may cause a murmur related entirely to relative pulmonic stenosis. If significant left ventricular volume overload occurs the mitral valve may become incompetent and a holosystolic murmur of mitral regurgitation may be evident over the left apex. The rare trabecular (muscular) VSD also may create a systolic murmur over the left or right apex. If significant cardiomegaly develops, atrial and ventricular premature complexes, or even atrial fibrillation, may be recognized. A holodiastolic murmur of aortic regurgitation indicates prolapse of an aortic cusp and the likelihood that the lesion is relatively large. Substantial aortic regurgitation is associated with a hyperdynamic arterial pulse. The VSD associated with pulmonary atresia or persistent truncus arteriosus may not create a substantial murmur, but the increased flow through the dilated single vessel usually creates a loud ejection murmur over each side of the chest.

Diagnostic Studies

Diagnostic studies confirm the lesion and, importantly, assess the hemodynamic burden. Noninvasive studies are sufficient for diagnosis in almost every case, and cardiac catheterization has become unnecessary except in rare instances. The performance history is a useful overall indicator of impact and the horse with an excellent work history is unlikely to have a large defect. The ECG is unreliable for diagnosing cardiomegaly in horses, but is indicated in the setting of an arrhythmia. Thoracic radiography can be useful in foals to demonstrate cardiomegaly, the pulmonary circulation, and the lungs and pleural space (see Figure 11.3-3). Two-dimensional echocardiography and color Doppler imaging establish the diagnosis. M-mode studies and spectral Doppler examinations are useful for assessing the hemodynamic burden of the defect.

Two-dimensional echocardiography successfully delineates the VSD in virtually all cases provided sufficient imaging planes are obtained (see Figure 11.3-4). Collection of long axis images of the left ventricular outflow tract and aortic valve is important, in addition to short axis images at the level of the left ventricular outflow tract, just below the aortic leaflets. The typical paramembranous defect appears under the aortic valve and adjacent to the septal leaflet of the tricuspid valve. A true defect is characterized by a relatively echogenic tissue interface, whereas an area of false echo dropout tends to be gradual. Most defects can be imaged in orthogonal (long axis/short axis) planes. The right coronary artery of the horse is relatively large and may be confused with a subarterial (supracristal) VSD. An inlet VSD (ventral

to the septal tricuspid valve) may not be easily seen in standard planes. Tipped or oblique views that show both atrioventricular valves may be required. Similarly, finding a muscular, apical, or small subarterial defect requires more imaging experience and is assisted by color Doppler studies.

Attempts should be made to identify the largest diameter of the defect in complementary planes and compare this with the size of the aorta because orifice size is an important prognostic factor. Although limitations exist to 2-D sizing of the VSD, a defect exceeding 2.5 cm in diameter or a VSD/aortic root diameter of more than 0.4 identifies a large defect with greater likelihood of clinical signs. Furthermore, 2-D or M-mode evidence of left-sided cardiac dilatation, right ventricular enlargement, or marked dilation of the main pulmonary artery suggest a hemodynamically-significant VSD and one more likely to impact performance or survival.

Identification of shunting across a VSD is best made using color Doppler studies. Typically a high-velocity, turbulent flow enters the right ventricle during systole with low velocity, uniform color shunting noted during diastole. Color Doppler imaging is extremely helpful for identifying a VSD with an atypical location and also may identify aortic regurgitation in some horses. Continuous wave Doppler is used to estimate the pressure difference between the two ventricles, as velocity (in meters/sec) is proportional to the instantaneous pressure difference across the ventricles ($\Delta P = 4V^2$). A relatively small VSD is "restrictive" to flow and the peak shunt velocity generally exceeds 4.5 m/second, assuming proper alignment to shunt flow. Should pulmonary hypertension develop related to increased pulmonary flow, left heart failure, or pulmonary vascular injury, the velocity of left-to-right shunting is lower, and a high velocity jet of tricuspid regurgitation (>3.5 m/sec) may be identified.

Prognosis and Management

Potential outcomes of the isolated VSD include the following:

1. Tolerance of the lesion
2. Partial or complete closure of a VSD by adherence of the septal tricuspid leaflet, fibrous tissue, right ventricular hypertrophy, or aortic valve prolapse
3. Progressive aortic regurgitation
4. Atrial fibrillation
5. Left-sided or biventricular CHF
6. Pulmonary hypertension (with left to right shunting)
7. Reversal of the shunt with development of arterial hypoxemia and cyanosis

The latter would be caused by either severe pulmonary vascular disease (Eisenmenger's physiology) or fibromuscular obstruction in the right ventricular outlet leading to subpulmonic stenosis. The horse with a relatively small diameter paramembranous defect, high-velocity left-to-right shunt, mild cardiomegaly, relatively normal right ventricular cavity, and normal heart rhythm probably has a restrictive VSD that will be well-tolerated. Most of these animals can perform sufficiently in the show ring, as a hunter-jumper, or even as an endurance or racehorse. Large defects that are associated with echocardiographic evidence of moderate to severe cardiomegaly, right ventricular hypertrophy, aortic root prolapse, or Doppler evidence of pul-

monary hypertension are prone to complications and carry a less favorable prognosis for performance or life regardless of current clinical signs.

Definitive therapy for VSD involves cardiopulmonary bypass surgery and is impractical. Surgical banding of the pulmonary artery elevates right ventricular pressures and reduces left-to-right shunting; however, this procedure also limits cardiac output and is not advised. Should CHF or atrial fibrillation develop, medical therapy can be considered in selected cases, but even if the response to treatment is good, the horse should not be used. This involves daily treatment with digoxin and furosemide (+/- an angiotensin converting enzyme inhibitor if economics are not an issue). Treatment of CHF is described in Chapter 11.6. In this author's opinion, breeding of affected animals should be discouraged, especially in Arabian horses.

TETRALOGY OF FALLOT

Pathology

The tetralogy of Fallot is one of the more common congenital cardiac anomalies in foals responsible for right-to-left shunting with arterial desaturation and cyanosis. The four lesions are large paramembranous VSD, right ventricular outflow tract obstruction, cranial and rightward (dextro-) positioning of the aorta with overriding of the septal defect, and right ventricular hypertrophy. Outflow obstruction can be due to subvalvular fibromuscular obstruction, valvular pul-

monic stenosis, or hypoplasia of the pulmonary artery. Ventricular hypertrophy is caused by right ventricular outflow obstruction and the large, unrestrictive, VSD that functionally creates a "common ventricle."

Blood leaves the heart along the path of least resistance, and pulmonary flow depends on the severity of right ventricular outflow tract stenosis. As previously discussed, the degree of cyanosis and severity of clinical signs depends on the volume of blood traversing the lungs. In some horses, a PDA is also present (pentalogy of Fallot) and this defect reduces signs by increasing pulmonary flow, left heart filling, and systemic arterial hemoglobin saturation.

Diagnostic Studies

Affected foals are usually smaller than normal, lethargic, and intolerant of exercise. Cyanosis is most evident after exercise but is variably present at rest. Arterial blood gas analysis demonstrates hypoxemia with normal or reduced PCO_2 . Auscultation is typically characterized by a loud systolic murmur over the pulmonic valve area on the left side caused by subpulmonic stenosis. The second heart sound is usually unremarkable. Although polycythemia can be significant, it is usually mild, even when arterial oxygen tensions fall to 50 to 70 mm Hg.

Echocardiographic evaluation is diagnostic and reveals a large, unrestrictive VSD, right ventricular outflow tract obstruction, malalignment and overriding of the aortic root, and right ventricular hypertrophy (Figure 11.3-5).

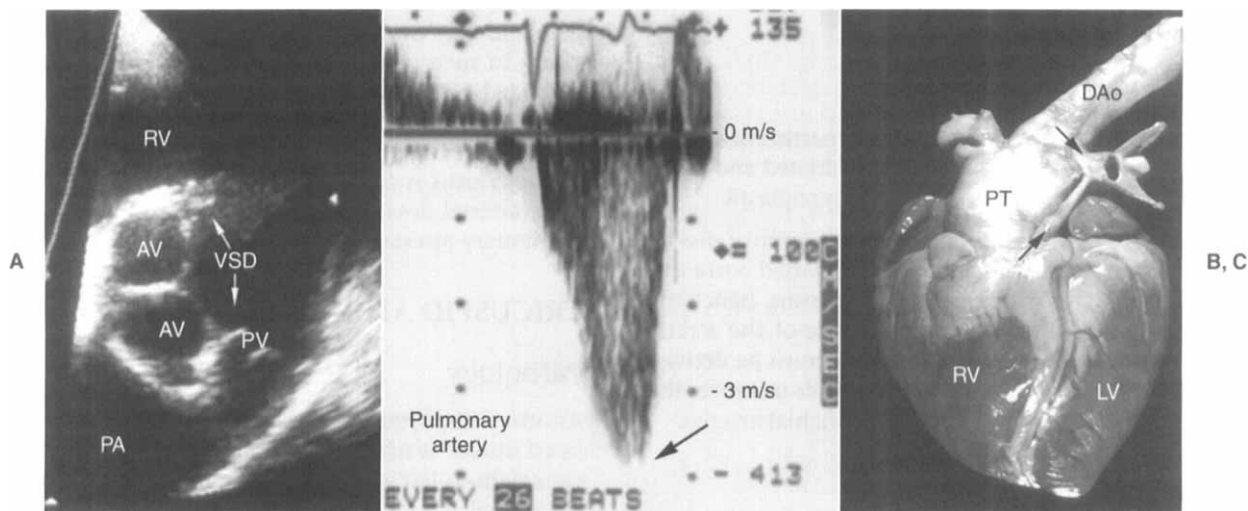


Figure 11.3-5 Tetralogy of Fallot. **A**, Echocardiogram from a filly with tetralogy of Fallot. The image plane shows the right ventricle, right ventricular outlet with stenotic (hypoplastic) pulmonary valves (PV), and post-stenotic dilation of the pulmonary artery (PA). There is a very large ventricular septal defect (VSD; arrows) connecting the base of the dilated aorta with the right ventricle. Two aortic valve leaflets (AV) are evident in this off-angle plane. **B**, Continuous-wave Doppler echocardiogram from a horse with tetralogy of Fallot. The Doppler study demonstrates pulmonary stenosis. High-velocity systolic flow is evident, exceeding 4 m/sec. Velocity scale is to the right; ECG at the top. **C**, Left lateral view of a heart obtained from a foal that died from pulmonary atresia, the "exaggerated" form of tetralogy of Fallot. Because of unequal septation of the truncus arteriosus, a markedly dilated aorta (pseudotruncus arteriosus = PT) and a rudimentary, imperforate main pulmonary artery (lower arrow) are present. Atresia of the pulmonary valve was evident on opening the heart. Pulmonary artery flow was derived from the ductus arteriosus (upper arrow), which serves two underdeveloped pulmonary arteries. DAo, Descending aorta; RV, right ventricle; LV, left ventricle.

Shunting can be identified by color Doppler or saline contrast echocardiography. An injection of agitated saline into the jugular vein results in a positive contrast echocardiogram and similar to the color Doppler study discloses the right-to-left or bidirectional shunt. Conventional spectral Doppler studies can be used to delineate the shunt (typically bidirectional, low-velocity flow of less than 2 m/sec) and right ventricular outflow obstruction (high velocity flow exceeding 4 m/sec).

Prognosis and Management

Although it is possible for horses to live for a number of years with tetralogy of Fallot, most affected animals are destroyed humanely as a result of the poor prognosis for life. Affected horses should not be used or bred if they survive to maturity. Tetralogy of Fallot must be distinguished from other causes of cyanotic heart conditions, including tricuspid atresia, pulmonary atresia with VSD, D-transposition of the great vessels, and double-outlet right ventricle with pulmonary stenosis.

PULMONARY ATRESIA WITH VENTRICULAR SEPTAL DEFECT

Pathology

Pulmonary atresia with VSD is rare, having been observed most often in Arabian foals (see Figure 11.3-5). This malformation represents the exaggerated form of tetralogy of Fallot, with the following findings:

1. The right ventricular outlet is atretic.
2. The right ventricle hypertrophied.
3. A large malalignment VSD is present.
4. The fetal truncus arteriosus has been partitioned so unequally that the aorta is markedly dilated and the pulmonary trunk atretic or severely hypoplastic.

Without careful ultrasound studies (or necropsy dissection) of the pulmonary circulation, the dilated aorta can be mistaken for a persistent truncus arteriosus, hence the moniker *pseudotruncus arteriosus*. Because of the atretic pulmonary valve, pulmonary blood flow must be derived either from a PDA or the aorta. In the latter instance, the systemic collaterals are usually from bronchial arteries.

Diagnostic Studies

The diagnosis of pulmonary atresia usually is prompted by the findings of cyanosis, cardiac murmur, and stunting in a foal or weanling and is confirmed by echocardiography. Careful echocardiographic studies can identify the main lesions: concentric hypertrophy of the right ventricle, unrestrictive VSD, dilated malaligned great vessel (the aorta), and inability to identify the pulmonary valve in the rudimentary right ventricular outflow tract (although a small pouch may be seen). Careful ultrasound examination of the ascending aorta and aortic arch from the right and left sides of the thorax fails to reveal a normal origin for the pulmonary trunk; however, the bifurcation of the pulmonary artery can usually be found from a cranial imaging position, and continuous flow into the vessel

documented by pulsed wave Doppler echocardiography. The origin of pulmonary flow is typically from the ductus arteriosus or a large collateral systemic artery.

PERSISTENT TRUNCUS ARTERIOSUS

Pathology

The clinical findings of persistent truncus arteriosus can resemble those of pulmonary atresia, but this depends on the magnitude of pulmonary blood flow. In this condition the fetal truncus never partitions and both ventricles continue to develop, communicating with the truncus arteriosus across a large VSD. Systemic, coronary, and pulmonary arterial flows each arise from the truncus, which is guarded by a truncal valve (which can be incompetent or stenotic). Pulmonary blood flow originates from one or more pulmonary arteries, which arise directly from the truncus arteriosus in one of three general ways (types I, II, III).

Diagnostic Studies

With careful ultrasound examination, the origin of the pulmonary arteries can be identified and the condition distinguished from pulmonary atresia with VSD. Furthermore in some cases an abnormal truncal valve (with four leaflets) suggests the diagnosis. If the pulmonary artery origins are not stenotic and if pulmonary vascular resistance remains relatively low, the clinical condition resembles a left-to-right shunt, except for right-to-left mixing of blood across the VSD. However the degree of arterial hypoxemia may not be severe and cyanosis may not be obvious. In such cases, development to maturity is possible provided CHF does not occur from unrestricted pulmonary flow and volume overload of the left ventricle. Conversely, high pulmonary vascular resistance in truncus arteriosus is associated with diminished pulmonary flow, arterial desaturation, and findings more similar to pulmonary atresia as discussed previously.

TRICUSPID ATRESIA

Pathology

Another important differential diagnosis for cyanotic heart disease is tricuspid atresia, a malformation that dictates right-to-left shunting of systemic venous blood at the atrial level. The atrial shunt may be across a true ASD or a patent foramen ovale. Because all venous return must mix in the left atrium, this malformation generally causes marked hypoxemia with cyanosis. Affected foals rarely survive to weanling age unless a VSD and functional right ventricular outflow tract are present. Otherwise, pulmonary flow must come from a ductus arteriosus or systemic collaterals (e.g., bronchial arteries).

Diagnostic Studies

Most foals are stunted, nurse poorly, and exhibit severe exercise intolerance and cyanosis at rest. Arterial oxygen tension can be very low (40 to 60 mm Hg). Echocardiography reveals a very dilated right atrium and coronary si-

nus, atretic tricuspid valve, and rudimentary right ventricle (larger if there is a functional left to right shunting VSD). Atrial shunting that allows systemic venous return to empty into the left atrium must be observed; a VSD may be present. Abnormal flow patterns can be verified by contrast or color Doppler echocardiography. Prognosis is grave.

ATRIAL SEPTAL DEFECTS

Pathology

Atrial septal defects and endocardial cushion defects are uncommon in foals. As indicated earlier, an ASD may involve different portions of the atrial septum (see Figure 11.3-1). Abnormal atrial septal patency is more likely to be observed with complex congenital cardiac defects, particularly when tricuspid or pulmonary atresia is present. An isolated ASD may be clinically insignificant, with no significant murmur or clinical signs. Moderate to good exercise capacity may be expected because left-to-right shunting decreases as the systemic to pulmonary vascular resistance ratio declines with exercise. In the case of a large ASD, left-to-right shunting leads to right-sided volume overload and pulmonary overcirculation. Such defects are visible echocardiographically, and Doppler echocardiography can confirm the direction of the shunt and estimate its severity. Atrial fibrillation has been observed in conjunction with ASD.

Complete endocardial cushion defects are rarely seen but are serious and usually lead to CHF or atrial fibrillation at an early age. This developmental defect typically consists of a large ASD of the primum and atrioventricular septum, a common atrioventricular valve leaflet, and a defect in the inlet portion of the ventricular septum. The ventricles may be partitioned normally, unequally with one rudimentary ventricular chamber, or not at all, creating a single ventricle. In the most severe cases there is a common atrioventricular canal, single large atrioventricular valve, and common single ventricle from which both great vessels exit.

Pathophysiology

The clinical signs of a complete endocardial cushion defect are variable. The foal with an unobstructed outlet to the pulmonary arteries is hemodynamically similar to one with a large VSD. When a common ventricle is present, varying degrees of cyanosis may be observed. A systolic murmur is typical and may reflect flow across the VSD, left-to-right shunting (relative pulmonary stenosis), or atrioventricular valve regurgitation.

Diagnostic Studies

An echocardiographic evaluation reveals an ASD involving the primum portion of the atrial septum, a VSD involving the muscular, inlet segment of the interventricular septum, and malformed atrioventricular valves. Doppler echocardiography reveals the intracardiac shunts and AV valvular regurgitation. CHF may supervene. The prognosis is poor.

PATENT DUCTUS ARTERIOSUS

Pathology

Patent ductus arteriosus (PDA) is a rare isolated congenital cardiac defect in foals and is detected most frequently in combination with other, more complex malformations. A continuous murmur from a PDA might be evident up to 72 hours after birth; thereafter the ductus should close functionally. If the ductus arteriosus remains patent, a left-to-right shunt from the aorta to pulmonary artery occurs. Theoretically, premature foals, foals with persistent pulmonary hypertension, and foals whose dams have been given prostaglandin inhibitors may be more susceptible to the development of a PDA.

The clinical signs depend on the magnitude of the shunting through the PDA, which is determined by its resistance and that of the pulmonary circulation. Physical examination findings include a continuous "machinery" murmur over the left craniodorsal cardiac border and bounding arterial pulses.

Diagnostic Studies

Echocardiography reveals pulmonary artery, LA, and LV volume overload with the severity of these findings commensurate with the magnitude of the shunt. Direct visualization of the PDA is not always possible by 2-D echocardiography, because the ductus arteriosus may be hidden from view by the overlying lung. Ductal flow is best identified from the left cranial imaging planes. Doppler studies demonstrate continuous high-velocity, turbulent flow, toward the main pulmonary artery. When PDA is diagnosed, the heart should be evaluated carefully for other congenital cardiac disease before surgical correction is considered. Late complications of this lesion include rupture of the pulmonary artery and atrial fibrillation.

Supplemental Readings

- Anderson RH: Nomenclature and classification: sequential Segmental Analysis. In Moller JH, Hoffman JIE (eds): *Pediatric Cardiovascular Medicine*, New York, Churchill Livingstone, 2000.
- Bayly WM, Reed SM, Leathers CW et al: Multiple congenital heart anomalies in five Arabian foals. *J Am Vet Med Assoc* 1982; 181:684-689.
- Bonagura JD, Reef V: Cardiovascular diseases. In Reed S, Bayly W (eds): *Textbook of Equine Internal Medicine*, Philadelphia, WB Saunders, 1998.
- Crowe MW, Swerczek TW: Equine congenital defects. *Am J Vet Res* 1985; 46:353.
- Leipold HW, Saperstein G, Woollen NE: Congenital defects in foals. In Smith BP (ed): *Large Animal Internal Medicine*, St Louis, Mosby, 1990.
- Reef VB: Cardiovascular disease in the equine neonate. *Vet Clin North Am Equine Pract* 1985; 1:117-129.
- Reef VB: Evaluation of ventricular septal defects in horses using two-dimensional and Doppler echocardiography. *Equine Vet J Suppl* 1995; 19:86-95.
- Rooney JR, Franks WC: Congenital cardiac anomalies in horses. *Vet Pathol* 1964; 1:454-464.
- Van Praagh R: Nomenclature and classification: morphologic and segmental approach to diagnosis. In Moller JH, Hoffman JIE (eds): *Pediatric Cardiovascular Medicine*, New York, Churchill Livingstone, 2000.

CHAPTER 11.4

Cardiac Dysrhythmias

I. MARK BOWEN

London, England

Cardiac dysrhythmias are a common finding in horses; however, the majority are physiologic in nature and occur in normal horses. With the exception of atrial fibrillation, pathologic dysrhythmias are most likely to occur in horses with underlying cardiac or gastrointestinal (GI) disease. Clinical signs related to dysrhythmias are highly variable. Although physiologic dysrhythmias are not associated with clinical abnormalities, horses with pathologic dysrhythmias may present with clinical signs ranging from decreased exercise tolerance to distress or collapse, but horses may also present without overt clinical signs related to cardiac dysfunction. Persistent dysrhythmias may be detected during a thorough cardiac auscultation and clinical examination, however, to accurately diagnose and treat rhythm disturbances an electrocardiogram (ECG) is essential. Veterinarians have a duty not only to diagnose and treat horses with cardiac dysrhythmias but also to provide information regarding the suitability of the horse for continued riding.

ELECTROCARDIOGRAPHY

Three basic types of ECG devices are available. The type of device needed to diagnose a given dysrhythmia depends on the frequency and persistence of the rhythm disturbance. Paper trace ECGs that are acquired horseside produce an instantaneous display while the device is attached to the horse; this is the most frequently obtained type of ECG. Paper trace ECGs are most useful to document persistent or frequent dysrhythmias, however, physiologic dysrhythmias may be abolished by restraint and handling of the animal. Continuous ambulatory (Holter) ECGs record the ECG during a prolonged period that ranges from 1 hour to several days. The data are stored on the device and then analyzed retrospectively. Continuous ambulatory ECGs are most useful to document infrequent or intermittent dysrhythmias, with the advantages that the horse can be returned to its normal environment where clinical signs have previously been documented. Holter monitoring can be used when the horse is at rest and while exercising. The main disadvantage to this method is that the ECG cannot be used for intervention because the ECG information is not available instantaneously. Telemetric ECGs combine the functionality of both of these devices in that the ECG signal is transmitted and displayed at a distant location so that the animal can be assessed in its natural environment. However, a real-time display is also available so that appropriate interven-

tion can be initiated immediately as needed. Telemetric ECGs are useful for monitoring horses in an intensive care situation or at exercise, and appropriate treatment can be applied while the ECG is being observed.

Obtaining a Diagnostic Electrocardiogram

Several lead systems exist for recording an ECG, and a base-apex lead system is usually sufficient; it produces large deflections and is the least affected by movement. The left arm (LA) electrode is placed over the heart on the left side, just above the point of the elbow. The right arm (RA) electrode (negative) is placed in the right jugular groove, two thirds down the neck. The right leg (ground) electrode (RL) can be placed over the body distant from the heart. Many battery-operated units have only two electrodes because no ground is required. Limb leads can accurately diagnose some dysrhythmias but are rarely necessary. During ambulatory recordings, chest lead systems are required so that the electrodes may be fixed under a girth to prevent movement artifacts. Chapters 11.1 and 11.2 detail electrocardiography further.

Interpretation of the Electrocardiogram

Interpretation of a diagnostic-quality ECG includes assessment of the heart rate (bradycardic, tachycardic, or normal), rhythm (regular or irregular), and origin of ventricular depolarization (atrial, supraventricular or ventricular). Although normal values for P wave and QRS complex height and duration have been published, they have little clinical value. In addition, T wave changes are common in horses and may come and go in the same animal during a period of time; thus care should be taken not to overinterpret the ECG. Atrial complexes (Figure 11.4-1, A) have a reasonable PR interval (normal 0.22-0.56 seconds) and have narrow upright QRS complexes (negative in lead I with a base-apex lead system). Supraventricular complexes have no preceding P wave, but have a narrow upright QRS complex, as with atrial complexes (see Figure 11.4-1, B). Ventricular complexes have no preceding P wave, or a preceding P wave with an unusually short PR interval (see Figure 11.4-1, C) and have a wide QRS complex. Ventricular complexes have T waves that differ markedly from supraventricular complexes, representing abnormal repolarization of the ventricles. Junctional complexes have supraventricular morphology, but the P wave is superimposed on the QRS complex.

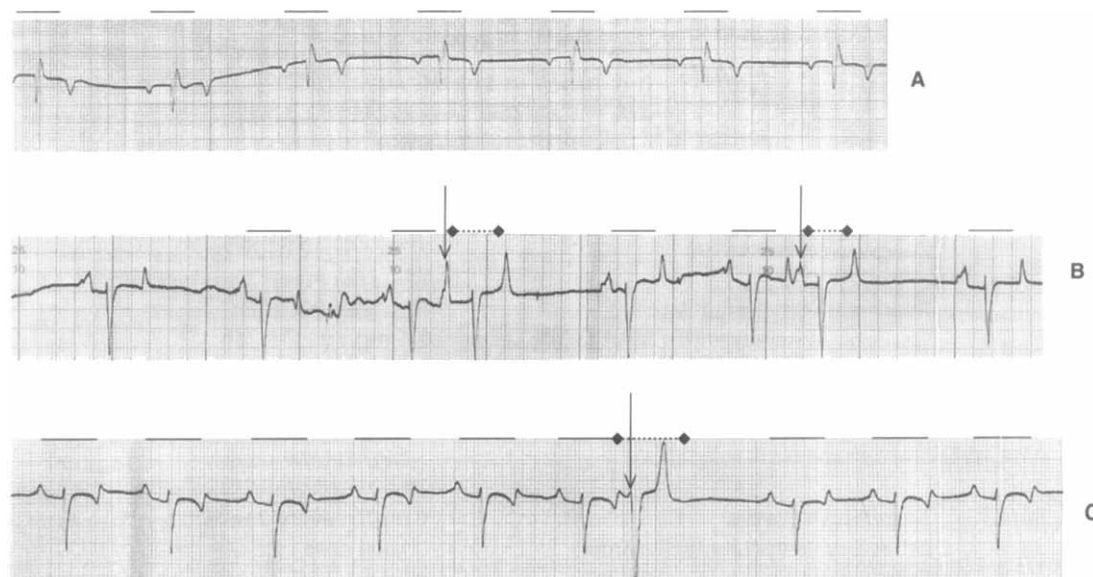


Figure 11.4-1 Identification of normal sinus rhythm, supraventricular and ventricular depolarizations from an ECG. **A**, Base-apex electrocardiogram (ECG) demonstrating normal sinus rhythm, with normal regular P waves and QRS complexes. **B**, Base-apex ECG from a 9-year-old pony gelding that demonstrates two supraventricular premature depolarizations (arrow) with abnormal premature P wave morphology and normal QRS complex morphology. In the first example, the P wave is hidden within an abnormal T wave from the preceding cardiac cycle. **C**, Base-apex ECG from an 8-year-old Thoroughbred gelding with isolated ventricular premature depolarizations (VPD; arrow). Note that VPD has wide QRS with abnormal T wave morphology and is followed by a compensatory pause. Horizontal solid lines represent normal cardiac cycle; dashed lines represent premature cardiac cycles.

Further Investigations

Once the presence of a dysrhythmia has been documented, it is essential to determine its significance, to identify any underlying disease, and to consider appropriate therapy. Differentiation between physiologic and pathologic dysrhythmias is essential, because the former do not require intervention. Also, some dysrhythmias may be an incidental finding that have no impact on the horse's presenting complaint and may resolve without specific therapy. In all cases of pathologic dysrhythmias, efforts to document an underlying cause are essential. Electrolyte or metabolic abnormalities are particularly important to identify, because correction of these derangements may correct the dysrhythmia and specific antidysrhythmic therapy may fail unless the underlying cause is addressed. However, in the case of life-threatening dysrhythmias antidysrhythmic therapy may be attempted before the underlying cause is determined. Table 11.4-1 summarizes drugs and dosages commonly used as antidysrhythmic agents in the horse. Laboratory determination of serum electrolytes, including ionized calcium and magnesium and serum potassium concentrations may be useful. Many dysrhythmias that require therapy will be refractory to treatment while severe electrolyte and acid-base abnormalities exist, and some antidysrhythmic agents are unlikely to be beneficial in the presence of acid-base and electrolyte abnormalities. Determination of serum cardiac troponin I (cTnI) concentrations and serum

activities of the cardiac isoenzymes of lactate dehydrogenase (LDH), α -hydroxybutyrate dehydrogenase (α -HBDH) and creatine kinase (CK-MB) can be useful to document myocardial necrosis or inflammation. Echocardiography is necessary to identify underlying myocardial disease, cardiac enlargement, or valvular pathology. In particular, ventricular dysrhythmias have been identified in horses with myocardial failure and severe aortic insufficiency, whereas atrial fibrillation may be associated with left atrial enlargement secondary to mitral valve regurgitation.

PHYSIOLOGIC DYSRHYTHMIAS

Physiologic bradydysrhythmias are particularly common in the horse and are caused by the high vagal tone in the resting horse. This condition is resolved by removal of the vagal influence, either pharmacologically with atropine or glycopyrrolate, or physiologically with exercise or stress. These bradydysrhythmias are not associated with cardiac disease; therefore treatment is not required. Occasionally these dysrhythmias will persist during exercise and are then characterized as pathologic dysrhythmias.

Atrioventricular Block

First-degree atrioventricular (AV) block is a physiologic lengthening of the PR interval and is resolved by exercise. Second-degree AV block is the most common physiologic

Table 11.4-1
Doses of Drugs Used to Treat Cardiac Dysrhythmias in the Horse

Drug	Indication	Dose
atropine	Bradycardia of vagal origin	0.01-0.2 mg/kg IV or SQ
bretylum	Refractory ventricular fibrillation	3-5 mg/kg IV
digoxin	Congestive heart failure	2.2 µg/kg IV q12h or 11 µg/kg PO q12h as required
enalapril	Treatment of atrial fibrillation	11 µg/kg PO q12h
glycopyrrrolate	Vasodilation in congestive heart failure	0.5 mg/kg PO q24h
hyoscine	Bradycardia of vagal origin	5 µg/kg IV
lidocaine	Bradycardia of vagal origin	0.14 mg/kg IV
	Ventricular tachycardia	0.5 mg/kg IV every 5 minutes; not to exceed 2-4 mg/kg total dose
magnesium sulfate	<i>Torsades des pointes</i>	20-50 µg/kg/min IV infusion
	Refractory ventricular tachycardia	4 mg/kg every 2 minutes; not to exceed 50 mg/kg total dose
phenylephrine	Critical maintenance of perfusion	Infusion 0.1-0.2 µg/kg/min IV; not to exceed 0.01 mg/kg total dose
phenytoin	Digoxin-induced ventricular tachycardia	7.5 mg/kg IV or 10 mg/kg PO q24h
procainamide	Ventricular tachycardia	1 mg/kg/min IV; not to exceed 20 mg/kg total dose
propafenone	Ventricular tachycardia	0.5-1 mg/kg IV during 5 minutes
propranolol	Refractory ventricular and supraventricular tachycardia (quinidine toxicity)	0.03- 0.16 mg/kg IV q12h 0.38-0.78 mg/kg PO q8h
quinidine gluconate	Acute onset atrial fibrillation	1.1-2.2 mg/kg IV q10 minutes; not to exceed 12 mg/kg total dose
quinidine sulfate	Ventricular tachycardia	
	Atrial fibrillation	22 mg/kg by nasogastric tube q2h for 6 doses

IV, Intravenous; SQ, subcutaneous; q12h, every 12 hours; PO, by mouth.

bradycardia in the horse. Auscultation reveals the presence of a regular irregularity, with a normal beat-to-beat interval but occasional missed beats. A solitary fourth heart sound may be audible in the prolonged pause. Occasionally two or three consecutive beats may be dropped. The dysrhythmia arises from the predominance of vagal tone manifested at the AV node, as opposed to the sinoatrial node. The ECG shows normal atrial complexes with blocked P waves, which have no associated QRS complex (Figure 11.4-2, A). Physiologic second-degree AV block is abolished by exercise, although may return rapidly as the horse stops exercising. Occasionally long pauses will be terminated by ventricular escape complexes, which are a normal electrophysiologic response of the ventricular pacemaker. Because advanced second-degree AV block associated with clinical signs such as collapse can indicate cardiac disease (e.g., myocarditis or myocardial fibrosis), further investigations are recommended to determine a therapeutic protocol.

Other Physiologic Bradycardias

Respiratory sinus arrhythmia is less marked in the horse than other species because of the vagal influence on the AV node. Auscultation reveals an irregular cardiac rhythm, with shortening and lengthening of the beat-to-

beat interval. The ECG shows a cyclic fluctuation in RR intervals that occur in time with the respiratory cycle (see Figure 11.4-2, B). Wandering atrial pacemaker may occur alone or in combination with other physiologic bradycardias and is characterized by changing P wave morphology that occurs at a normal sinus rate. Sinoatrial block has long sinus pauses with normal atrial complexes; the ECG is similar to AV block except for the absence of P waves in the prolonged pauses (see Figure 11.4-2, C). Sinoatrial arrest is a profound form of sinoatrial block that lasts more than two PP intervals. These prolonged sinus pauses may be terminated by ventricular escape complexes that represent the lower rate of the ventricular pacemaker.

PATHOLOGIC BRADYDYSRHYTHMIAS

Atrioventricular Block

Pathologic second-degree AV block is uncommon in the horse and often occurs in association with myocardial inflammation, although it may also occur under general anesthesia without myocardial disease. Auscultation reveals a slow heart rate with prolonged pauses, and the rhythm may be regular or irregular. The electrocardiographic features of advanced second-degree AV block are P



Figure 11.4-2 Physiologic bradydysrhythmias of the horse. **A**, A postexercise electrocardiogram (ECG) from a 5-year-old Thoroughbred gelding demonstrating Mobitz type 1 (with lengthening of the PR interval) second-degree AV block. Dark arrows demonstrate P waves that are blocked by the atrioventricular node; open arrows show normal P waves, followed by QRS complexes. This dysrhythmia was resolved during exercise but returned within 2 minutes after the end of exercise. **B**, Ambulatory ECG from a 5-year-old Thoroughbred mare demonstrating respiratory sinus arrhythmia. Horizontal bars demonstrate the RR interval of the first cardiac cycle. **C**, Ambulatory ECG from the same horse as in B demonstrating sinus arrest, with a period without any atrial activity. Arrows demonstrate timing of expected P waves from preceding PP intervals. Both sinus arrhythmia and sinus arrest were abolished at exercise. Note all three ECGs have been obtained with ambulatory recording material by using a nonstandard lead system; hence the T waves appear very large in B and C.

waves with no QRS complexes that occur either during exercise or with more than three blocked P waves in association with collapse. The prolonged pauses may be terminated by ventricular escape complexes at a ventricular rate of 10 to 20 beats per minute (bpm). Third-degree AV block is a complete dissociation between atrial and ventricular electrical activity. The ventricular rate is usually rhythmic and occurs at a lower rate than the atrial rate. The ECG findings are of regular, wide QRS complexes with regular but unrelated P waves. P waves may be interposed over QRS complexes, giving the impression of an irregular atrial rate. Occasionally the ventricular response may be irregular (Figure 11.4-3) with long ventricular pauses, suggestive of pathology within the ventricular conduction system.

Horses with pathologic dysrhythmias that have the potential for life-threatening complications (e.g., low blood pressure, increase serum creatinine, collapse) may be treated with positive inotropes such as dobutamine. Vagolytic agents, such as atropine, will have no therapeutic effect. Possible investigations include determination of serum potassium concentrations, serum troponin concentrations, and activities of the cardiac isoenzymes. Hyperkalemia can be treated with infusions of dextrose and insulin to lower circulating potassium concentrations, as well as by correction of the underlying cause (e.g., bladder wall defects). If evidence exists of cardiac inflammation or myocardial necrosis, the use of corticosteroids is

sometimes beneficial. Horses with third-degree AV block and clinical signs of cardiac insufficiency can be managed by placement of a transvenous pacemaker. Although pacemaker technology has seen tremendous advances in the last few years, the use of dual-chamber dual-sensing pacemakers has not been fully evaluated to determine the suitability of treated horses for riding.

Atrial Fibrillation

Atrial fibrillation (AF) is the most common pathologic dysrhythmia in horses. Horses more often present with a normal to slow heart rate, although if AF occurs in horses with congestive heart failure, it will be present as a tachydysrhythmia.

Mechanisms of Atrial Fibrillation

AF occurs as a result of the development of reentrant pathways within the atrial myocardium. Heterogenicity of atrial myocyte refractory periods is a prerequisite for the development of AF, such that adjacent areas of myocardium are in a state of depolarization, absolute refractory periods, and relative refractory periods at any given time. Once initiated a critical atrial mass is required to sustain fibrillation. The horse is predisposed to AF because of predominant vagal tone that leads to variable refractory periods, as well as to a large myocardial mass, so that a normal horse is capable of sustaining AF. Therefore AF can

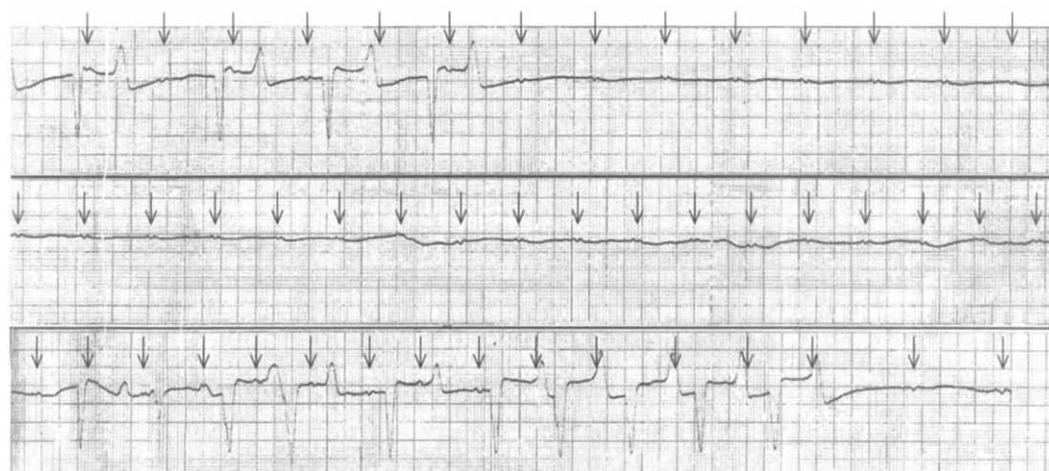


Figure 11.4-3 Base-apex electrocardiogram from a 10-year-old Arabian mare with third-degree atrioventricular block. Note the P waves (arrows) without associated QRS complexes and the wide ventricular escape complexes. Abnormal ventricular pacemaker function has resulted in irregular ventricular rate with periods of inactivity extending for as long as 30 seconds. This duration of ventricular arrest caused significant compromise to circulatory function and caused the mare to collapse. The condition was managed with the use of a transvenous single-chamber, fixed-rate pacemaker.

occur spontaneously without underlying heart disease (uncomplicated AF) or in horses with cardiac disease that results in atrial enlargement. Mitral valve disease is the most common cardiac lesion to result in AF, but severe tricuspid valve regurgitation can cause significant right atrial enlargement that leads to AF. Recent research in perfused rabbit hearts has suggested that stretch-activated ion channels may play an important role in the pathogenesis of AF, because AF can be induced more readily in the presence of increasing atrial stretch. The existence and importance of these channels in the development of naturally occurring AF in the horse has not been determined.

Paroxysmal AF is a less common condition wherein horses develop AF and revert to normal sinus rhythm spontaneously. It is an important differential diagnosis for horses with acute onset of poor performance, or collapse during exercise. Diagnosis is complicated by rapid conversion to sinus rhythm once exercise has stopped. In these cases, a diagnosis can only be made with the use of exercising electrocardiography.

Clinical Signs

Poor performance is the most common problem of horses that present with AF, and it is most evident in horses engaged in vigorous athletic activities. Pleasure horses may be able to perform their normal level of exercise without any evidence of compromise; this fact makes the time of onset of AF difficult to determine in these animals. Exercise-induced pulmonary hemorrhage occurs in a smaller number of cases of AF.

Diagnosis

Auscultation reveals an irregularly irregular pulse and cardiac rhythm with a normal or low heart rate. In contrast to horses with AV block no fourth heart sound is present in the prolonged pauses. Careful observation or palpation of the jugular pulse at the thoracic inlet will reveal a

biphasic, as opposed to the normal triphasic, pulse waveform. The diagnosis is confirmed by ECG, which demonstrates upright, narrow, supraventricular complexes, with an irregularly irregular RR interval and no preceding P waves. The baseline is marked by fibrillation waves (F waves) as shown in Figure 11.4-4, A. Further diagnostic techniques that can be considered are dependent on other clinical and historic findings. Echocardiography is necessary in horses that have concurrent cardiac murmurs in order to document valvular pathology and cardiac enlargement. In horses with paroxysmal AF serum, electrolytes should be measured and fractional electrolyte excretion determined, with particular reference to potassium and magnesium.

Prognosis

Conversion to normal sinus rhythm is the preferred outcome because it allows horses to return to their previous level of performance. Successful conversion depends on the duration of AF and the absence of structural cardiac disease. With careful case selection, a successful outcome can be achieved in approximately 85% of cases of uncomplicated AF. Duration of AF and the presence of underlying pathology are the most important predictors of successful conversion. Treatment of horses with AF of long duration or with significant cardiomegaly is unlikely to be successful. Because of the potentially life threatening complications of quinidine therapy, treatment of horses with a poor prognosis for conversion is rarely attempted. Horses with AF of less than 3 months duration have a good success rate for conversion to normal sinus rhythm, with a low rate of recurrence of AF (15%).

Further Investigations

Echocardiography should be performed in horses with AF in which cardiac murmurs can be heard. The aim of echocardiography is to document atrial enlargement to

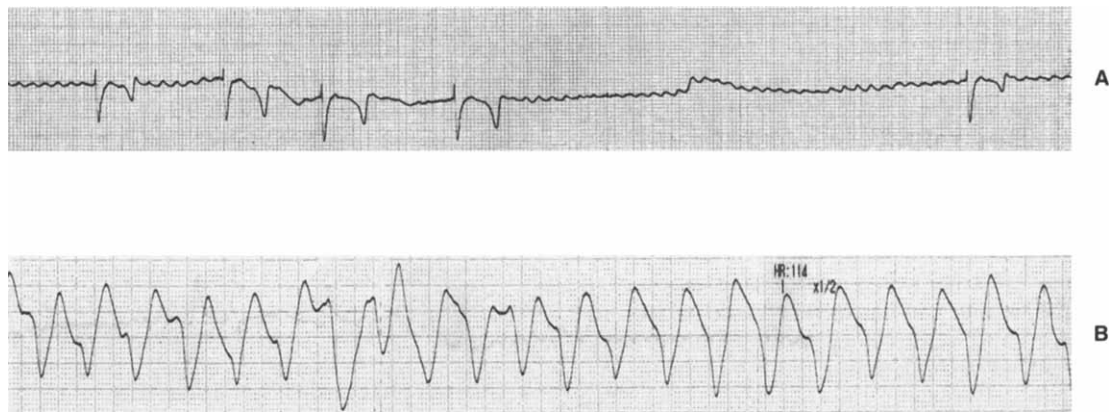


Figure 11.4-4 **A**, Base-apex electrocardiogram (ECG) from a 7-year-old gelding with atrial fibrillation, demonstrating fine F waves on the baseline with an absence of P waves. **B**, Ambulatory ECG from horse shown in A demonstrating *torsades-de-pointes* after administration of 330 mg/kg quinidine sulfate during 40 hours. The horse was treated with 5 boluses of 2 g of magnesium sulfate IV with 20 mg propranolol IV, which resulted in conversion to normal sinus rhythm. Note the widely fluctuating ventricular tachycardia with high heart rate.

identify horses in which treatment is unlikely to be successful. Left atrial enlargement secondary to mitral valve disease is the most common cause of secondary AF in the horse, although significant tricuspid regurgitation with right atrial enlargement, ventricular septal defects, and aortic valve regurgitation can also predispose to AF. Horses with a left atrial diameter greater than 14.8 cm are not likely to be converted successfully to normal sinus rhythm. Right atrial enlargement is difficult to quantify echocardiographically; thus specific guidelines are not available.

Treatment of Uncomplicated Atrial Fibrillation

Horses with AF of less than 1 day's duration, or horses that present with signs of noncardiac systemic disease do not require immediate treatment, because spontaneous conversion may occur. Horses undergoing anesthesia that have concurrent AF are not at a particularly increased risk of complications, thus conversion before anesthesia is not essential in life-threatening situations. It is advisable to avoid the use of α_2 -adrenergic agonist drugs such as xylazine and detomidine because they may add to the severity of the bradycardia.

Horses with an acute onset of uncomplicated AF of less than 7 days duration can be treated with quinidine gluconate at a dose of 1.1 to 2.2 mg/kg intravenously every 10 minutes until conversion to normal sinus rhythm, or until a total dose of 12 mg/kg has been administered. If this treatment is unsuccessful or unavailable an oral quinidine sulfate regime can be used. Horses with chronic uncomplicated AF are routinely treated by administration of quinidine sulfate through a nasogastric tube. Oral dosing should not be performed, because quinidine sulfate is irritating to the mucosa of the GI tract and causes oral ulcerations. The pharmacokinetics of quinidine are highly variable, therefore therapeutic drug monitoring is advisable. Monitoring is rarely available, however, thus recommendations are based on average pharmacokinetic data in the

horse. Electrocardiographic monitoring by telemetric ECG is recommended throughout the period of treatment, because drug-induced cardiac dysrhythmias can occur that may be fatal if left untreated. In addition, a paper trace, base-apex ECG should be obtained before each dose to document QRS prolongation, which is a dose-dependent effect of quinidine sulfate that can lead to ventricular tachycardia.

Several different treatment regimes exist for the use of quinidine sulfate in horses with AF. The following protocol is widely employed: quinidine is administered every 2 hours at a dose of 22 mg/kg until (1) normal sinus rhythm is achieved; (2) a total of five doses have been given; (3) significant QRS prolongation occurs to greater than 25% of the pretreatment duration; or (4) other life-threatening complications occur. In the event of significant QRS prolongation, the dosing interval is extended so that quinidine is readministered only after the QRS duration has returned to acceptable limits. If conversion has not occurred after the fifth dose, the dosing interval is adjusted based on serum concentrations of quinidine sulfate (2–5 $\mu\text{g/ml}$) or to a 6-hour interval. If successful conversion has not been achieved by the second day of treatment, digoxin at a dose of 11 $\mu\text{g/kg}$ orally is combined with the 6-hour quinidine doses. The rationale for the combination of quinidine and digoxin is that digoxin slows AV nodal conduction and hence offsets some of the proarrhythmic effects of quinidine. Both drugs are highly protein bound, thus coadministration can increase the effective plasma concentrations of both agents, which may increase the likelihood of adverse effects of either drug.

Complications of the Use of Quinidine Sulfate in the Horse

Quinidine sulfate can induce both cardiovascular and noncardiovascular side effects. The most common complications are noncardiac and include depression, paraphimosis, and colitis. These complications are usually self limiting

and stop after cessation of treatment. The development of colitis is not related to the dose of quinidine administered but, in some cases, the severity of colitis may necessitate discontinuation of therapy. Quinidine-induced colitis can be treated symptomatically with intravenous (IV) fluid therapy and GI protectants. Nasal mucosal edema and ataxia can occur at higher doses and are less common than GI side effects. Cardiovascular complications can be explained by three actions of quinidine sulfate—vagolytic effects, which can cause supraventricular tachycardia, prolongation of the action potential, which can cause ventricular tachycardia (Figure 11.4-4, B) and α -adrenoceptor antagonism, which can cause peripheral vasodilatation and hypotension.

Because of the potentially life-threatening dysrhythmias and the fact that these effects are not dose dependent, horses undergoing quinidine therapy should ideally have continuous electrocardiographic monitoring so that prompt intervention is possible. Horses that develop supraventricular tachycardia with a heart rate higher than 100 bpm should be treated with IV sodium bicarbonate to increase plasma protein binding and hence reduce the amount of free quinidine in circulation. IV digoxin will slow conduction through the AV node; if digoxin is unsuccessful in controlling heart rate propranolol can also be administered to further reduce the ventricular response rate. Horses that develop ventricular tachycardia during treatment should be treated with bicarbonate, propranolol, and magnesium sulfate. If the ventricular tachycardia appears unstable, IV lidocaine and/or procainamide can be administered. Hypotension can be managed by administration of IV crystalloids; if the condition is refractory, IV phenylephrine can be administered to improve pressures. A summary of emergency protocols for the treatment of quinidine sulfate-induced dysrhythmias is shown in Table 11.4-2.

Posttreatment Management

After treatment for atrial fibrillation most horses can return immediately to normal exercise. When possible, a continuous 24-hour ambulatory ECG (Holter monitor) can be used to document the incidence of atrial ectopy. Monitoring is important because horses with frequent atrial premature depolarizations are more likely to revert to AF. These horses should be rested for at least 1 month or until the ectopy resolves. Horses that revert to AF after treatment can undergo repeated treatment with the protocol described previously.

If treatment is not successful, not attempted, or the horse reverts to AF, the owner should be counseled as to the likely effect on performance and safety. Most horses with AF are considered safe to ride and can perform at reasonable levels of exercise, although their performance may be blunted. A small proportion of horses during exercise may develop paroxysmal ventricular tachycardia (Figure 11.4-5). The chance that a horse could collapse while being ridden may represent a significant risk to the rider.

Other Treatment Regimes for Atrial Fibrillation

Successful conversion to normal sinus rhythm is achieved in 85% to 90% of cases with appropriate case selection. Thus newer treatment modalities are under investigation in order to overcome the side effects of quinidine sulfate

Table 11.4-2

Management of Significant Side Effects of Quinidine Administration in the Horse

Toxic Effect	Treatment
Urticaria	Discontinuation of treatment; corticosteroids if severe
Upper respiratory tract obstruction	Dexamethasone 0.1 mg/kg IV; nasotracheal tube or tracheostomy if severe
Supraventricular Tachycardia	
Heart rate <100 bpm	Monitoring for signs of progression
Heart rate >100 bpm	Digoxin 2.2 μ g/kg IV
Heart rate >150 bpm	Digoxin 2.2 μ g/kg IV Sodium bicarbonate 1 mmol/kg <i>If unsuccessful:</i> Propranolol 0.03 mg/kg IV
Ventricular tachycardia	Sodium bicarbonate 1 mmol/kg Magnesium sulfate 4 mg/kg q2min; not to exceed 50 mg/kg total dose <i>If unsuccessful:</i> Lignocaine infusion 20-50 μ g/kg/min or 0.25-0.5 mg/kg slow IV q10min
Congestive heart failure	Digoxin 2.2 μ g/kg IV
Hypotension	<i>If severe or of the horse collapses,</i> phenylephrine infusion 0.1-.2 μ g/kg/min IV; total dose not to exceed 0.01 mg/kg

IV, Intravenous; q2min, every 2 minutes.

rather than improve conversion rates. The exception to this is with the development of drugs which block the activity of stretch-activated ion-channels, which may allow for successful conversion of horses with atrial enlargement. Currently no pharmacologic agents have been developed, and only one agent (GsMtx-4) has undergone *in vitro* assessment in the rabbit. Thus products such as this will not become available for therapeutic use for some time.

Quinidine salts. In contrast to equine AF, the management of human beings with AF requires chronic medication; hence there has been a trend to develop agents with a longer half-life than quinidine sulfate. These agents include quinidine bisulfate, which is bound to a plastic base to delay release in the GI tract, and quinidine polygalacturonate, which causes less GI irritation than the parent compound. Although these agents could be used for the treatment of horses with AF, no pharmacokinetic data are available to recommend suitable dosing intervals. The longer half-life that these agents have will increase the time needed to achieve steady-state concentrations; a longer half-life is contraindicated in the early stages of treatment. Indeed, quinidine sulfate is the pharmacologic agent of choice for

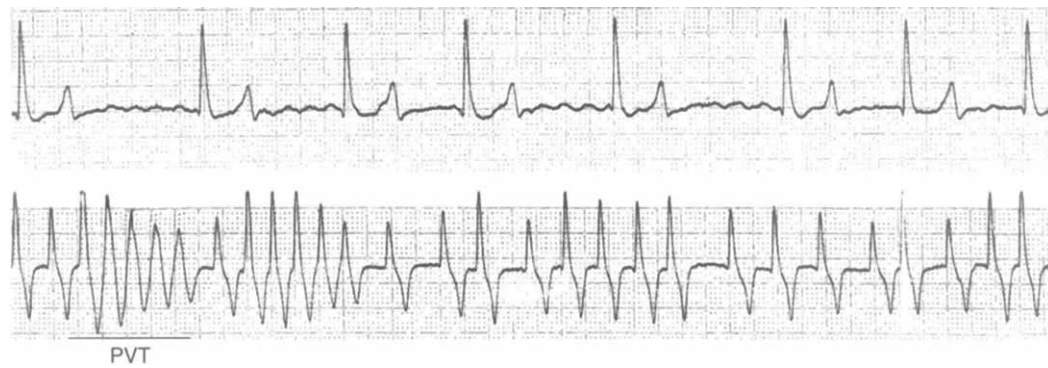


Figure 11.4-5 Ambulatory electrocardiogram recorded at rest and exercise for a 14-year-old Irish Draft gelding showing the presence of atrial fibrillation at rest (*top strip*) while at exercise paroxysmal ventricular tachycardia (PVT) was recorded (*lower strip*). Note the saw-tooth appearance demonstrating the R-on-T phenomenon in which the R wave is continuous with the T wave from the preceding complex. This dysrhythmia is potentially unstable and will compromise cardiac output as the result of poor ventricular filling.

initial therapy in humans before chronic medication with products with longer elimination half-lives. Substituting these agents into a quinidine sulfate protocol for use in the horse is potentially dangerous, because higher plasma concentrations will be achieved in the later stages of treatment.

Flecainide. Flecainide is a class IC antidysrhythmic agent; therefore, it has similarities with quinidine in blocking fast sodium channels. However, class IC drugs have powerful effects on the upstroke of the cardiac action potential and have an inhibitory effect on the Purkinje fiber system. These drugs cause QRS prolongation and heterogeneity of action potentials within the Purkinje system and surrounding myocardium, promoting further dysrhythmias. These proarrhythmic effects are exaggerated in the presence of left ventricular dysfunction, therefore these drugs are contraindicated in the presence of congestive heart failure.

IV infusion of flecainide to a mean total dose of 1.4 mg/kg has been shown to be effective in horses in terminating AF that was artificially induced by atrial pacing. An oral dose of 4 to 6 mg/kg achieves the same effective plasma concentrations of the drug. Peak concentrations are achieved more rapidly than with quinidine sulfate and the plasma half-life after oral administration is less variable between horses than with quinidine sulfate (mean flecainide time to maximum concentration [t_{max}] = 60 minutes compared with mean quinidine sulfate t_{max} = 146 minutes; mean flecainide half-life, 5.06 ± 1.45 compared with 6.65 ± 3.0 hours for quinidine sulfate). Thus, dosing intervals to maintain effective concentrations of flecainide would need to be shorter in order to maintain steady state concentrations. The main advantage of flecainide would be the lack of GI or vagolytic effects. However, flecainide cannot be recommended as a superior treatment to quinidine sulfate at present, because of the proarrhythmic effects that have been described in human beings. These proarrhythmic effects are caused by heterogeneity of Purkinje fiber conduction, therefore the incidence of ventricular tachycardia

may be greater than for quinidine sulfate. Furthermore, the differences in plasma glycoprotein binding would suggest that plasma alkalization would be ineffective in controlling drug-induced dysrhythmias that occur.

Direct current conversion. Direct current (DC) conversion is the treatment method of choice in humans with chronic AF. However, the use of monophasic DC conversion is unsuitable for use in large animals because of transthoracic impedance. Biphasic defibrillators can overcome this downfall and thus offer the greatest hope as a replacement for quinidine sulfate treatment in the horse. The procedure requires general anesthesia and transthoracic echocardiography to identify optimum placement for the paddles. Concurrent treatment with quinidine gluconate may be beneficial in promoting conversion and preventing relapse. Further evaluation of this technique is required before it will replace quinidine sulfate as the treatment of choice for equine AF.

Atrial Fibrillation in Horses with Congestive Heart Failure

Atrial fibrillation does not progress to cause congestive heart failure (CHF), although underlying pathologic processes that cause AF may also progress to cause CHF. Thus AF may be found in horses with CHF, although it is not a direct cause of cardiac failure. Cardiomegaly, especially left atrial enlargement, is the most common underlying cause of CHF and AF. Horses with CHF and AF have elevated heart rates (typically >60 bpm). Despite the presence of disease in the left side of the heart, horses often present with signs of right-sided heart failure with prominent jugular pulses that extend towards the ear and ventral edema. Horses rarely present with left-sided CHF with pulmonary edema, although this combination may occur in horses that develop acute onset left-sided heart failure such as toxin-induced myocardial disease. The aim of therapy for horses with AF and CHF is to control the ventricular rate to improve ventricular filling and cardiac

performance. These horses have a poor prognosis for conversion and quinidine sulfate is contraindicated because of its hypotensive effects. Therapeutic agents are used to control the ventricular response rate and to increase diastolic filling and hence improve cardiac output of affected horses. Thus digoxin can be used to control clinical signs of congestive heart failure, and can be combined with propranolol and/or verapamil to further control the ventricular rate. Therapeutic drug monitoring is recommended after 2 weeks of digoxin therapy to ensure that appropriate serum concentrations of the drug are achieved.

TACHYDYSRHYTHMIAS AND ECTOPIC BEATS

Supraventricular Ectopic Beats

Infrequent atrial premature depolarizations (APDs) can be detected in ambulatory ECG recordings from normal horses, whereas frequent APDs may occur in horses with cardiac or GI disease. In a study of horses with aortic valve regurgitation, APDs were identified in 30% of horses. Horses with frequent APDs may be at an increased risk of developing AF. APDs have the ECG characteristics of sinus complexes but occur prematurely within the cardiac cycle. The P wave morphology is usually different from the preceding complex and is usually followed by a normal QRS complex. Horses with frequent APDs should undergo determination of serum electrolytes and markers of cardiac inflammation. Treatment includes correction of any electrolyte abnormalities and the use of corticosteroids if evidence exists of myocarditis. In some horses, frequent APDs may resolve after rest at pasture.

Supraventricular Tachydysrhythmias

Supraventricular tachycardia (SVT; Figure 11.4-6) may occur in horses with AF and CHF, or in the presence of other cardiac or electrolyte abnormalities. SVT with a heart rate greater than 100 bpm and no underlying cardiac disease may be treated with quinidine gluconate or quinidine sulfate. In the presence of AF and CHF the aim of therapy is to control the ventricular rate to improve cardiac performance.

Digoxin

Digoxin is beneficial in the control of the ventricular rate in horses with supraventricular ectopy because it delays conduction through the AV node. This effect is achieved

through direct effects on the Na/K adenosine triphosphatase pump and through central vagomimetic effects. The inotropic effects of digoxin are complex and dependent on peripheral vascular tone and baroreceptor responsiveness. Therapeutic drug monitoring is recommended after five half-lives (3-6 days) to ensure that plasma concentrations are within the therapeutic range (0.5-2 ng/ml). Digoxin may induce tachydysrhythmias, which may be exacerbated by hypokalemia. Digoxin-induced dysrhythmias can be treated with phenytoin as discussed later in this chapter.

Ventricular Ectopic Beats

Ventricular dysrhythmias are commonly identified in horses with GI disease and underlying cardiac disease. Occasional ventricular ectopy can be identified in normal horses during continuous ambulatory monitoring and may be of no significance. However, frequent ectopy may indicate myocardial pathology or, in some cases, may increase in frequency and result in ventricular tachycardia. Thus frequent ventricular ectopy warrants further investigation. Ventricular tachydysrhythmias are the most common dysrhythmia to cause collapse in the horse, thus horses should be evaluated carefully to determine their suitability for ridden exercise. This evaluation involves determination of the frequency and severity of the dysrhythmia in the resting horse and while the horse is undertaking a prolonged period of exercise. Horses with ventricular ectopic beats that are infrequent (less than one per hour) or that are abolished with exercise, and have no other evidence of cardiac disease, are usually safe to be ridden, whereas horses with frequent isolated ventricular premature contractions (VPCs), paroxysms of ventricular tachycardia (VT), or VPCs that persist at exercise may result in collapse during exercise. Ventricular ectopy that develops only during maximal exercise may be related to upper airway obstruction and relative hypoxia; thus appropriate investigations are recommended.

Investigation of Ventricular Ectopy

Electrocardiography. To document the severity of ventricular ectopy in the resting horse, continuous ambulatory electrocardiography is useful to determine the true prevalence of this condition and to document any improvement after therapy. It can be useful to record the ECG while the horse is exercising to document the frequency of ectopy and provide information that can be used to determine the suitability of the horse for riding.



Figure 11.4-6 Base-apex electrocardiogram from a 10-year-old pony gelding with supraventricular tachycardia with a heart rate of 78 bpm. Note the P waves occur at irregular intervals but with normal QRS complexes. Some P waves are superimposed on the T wave of the preceding complex (arrow). The pony had myocarditis of unknown etiology.

Laboratory investigations. Ventricular ectopy may occur as the result of myocarditis or myocardial fibrosis; thus determination of serum activities of cardiac enzymes (LDH-1, α -HBDH, or CK-MB) or concentrations of cTnI can be used to document underlying myocardial disease. Evaluation of serum electrolyte disturbances, including measurement of ionized calcium and magnesium, is recommended. Hypokalemia and hypomagnesemia are most likely to be a cause of ventricular ectopy. Determination of electrolyte abnormalities is essential as these may affect the usefulness of specific antidysrhythmic agents such as lidocaine.

Echocardiography. Two-dimensional echocardiography is indicated in all forms of ventricular ectopy to document any areas of focal myocarditis or cardiomegaly. This information is useful to determine prognosis and thus identify which animals are suitable candidates for treatment. Horses with left ventricular enlargement and rapid VT in congestive heart failure have a poor prognosis.

Treatment of Horses with Ventricular Ectopic Beats

The aim of therapy in horses with ventricular ectopy is to reduce the incidence of ectopy to enable the horse to continue normal exercise. Treatment may consist of nonspecific therapy, correction of electrolyte abnormalities and, in the case of myocarditis, use of corticosteroids. Corticosteroids are sometimes useful in reducing the incidence of ectopy in horses with biochemical evidence of myocarditis. These horses should be rested until no further biochemical evidence exists of myocardial disease and the incidence of ectopy has reduced to less than one incidence of ectopy per hour.

Phenytoin. Specific therapy for horses with occasional ventricular ectopy is often unsuccessful, however, oral antidysrhythmic therapy can be instituted. Phenytoin is classically indicated for the control of digoxin and other glycoside-induced dysrhythmias, but it may also be of some benefit in the control of ventricular ectopy in the horse. Phenytoin (20-22 mg/kg PO q12h) has been evaluated in nine horses with ventricular ectopy. After four doses, ectopy was resolved in all horses. Oral dosing was adjusted to maintain an average serum concentration of 9.4 mg/ml. Sedation was observed at concentrations of 14.4 mg/ml and excitement at 18.7 mg/ml.

Other agents. Propafenone, a class IC antidysrhythmic agent, blocks fast sodium channels. Propafenone has provided little clinical benefit in horses and its kinetics have not been evaluated. It is rational to use angiotensin-converting enzyme (ACE) inhibitors such as ramipril and enalapril in the treatment of horses with ventricular ectopy and cardiac enlargement. In horses an association exists between aortic valve insufficiency, left ventricular enlargement, and ventricular ectopy. It has been hypothesized that during cardiac disease activation of a locally acting renin-angiotensin activating system (RAAS) is proarrhythmic. Pharmacologic intervention in this pathway by use of enalapril may reduce the incidence of ectopy. This author has successfully used enalapril to control the occurrence of ventricular ectopy in one horse that developed paroxysmal ventricular tachycardia during exercise. Few pharmacologic data exist on use of the ACE inhibitors in the horse, although enalapril (0.5

mg/kg PO q12-24h) has been used without side effects. Further validation is required before specific indications for the use of ACE inhibitors and propafenone can be identified.

Ventricular Tachydysrhythmias

In contrast to ventricular ectopy, ventricular tachydysrhythmias may have a direct effect on cardiac output and may destabilize into a more malignant dysrhythmia that results in death. Tachydysrhythmias can occur because of abnormal automaticity or may occur in horses with underlying cardiac or GI diseases. Electrolyte abnormalities such as hypokalemia and hypomagnesemia may predispose to ventricular tachydysrhythmia. Vascular catastrophe or myocardial dysfunction resulting from inflammation, enlargement, or fibrosis can also result in these dysfunctions.

Investigation of Ventricular Tachydysrhythmias

Although documentation of any underlying pathology is essential to determine both treatment and prognosis, a delay in therapy while investigations are undertaken may not be possible. If the rate of the tachydysrhythmia is low and no evidence exists of decreased circulatory function, investigations should include electrolyte determination and biochemical evaluation of myocardial disease and echocardiography, as discussed in the section on ventricular ectopy in this article. Horses in which specific antidysrhythmic therapy is indicated (see next section) may be treated immediately.

Treatment of Ventricular Tachydysrhythmias

Specific antidysrhythmic therapy is indicated in horses in which the ventricular rate is greater than 100 bpm, the complexes are polymorphic, evidence exists of decreased cardiac output (e.g., weakness, azotemia) or the rhythm is at risk of destabilizing into ventricular fibrillation. The R-on-T phenomenon (Figure 11.4-7) is the rhythm disturbance that may quickly destabilize into fibrillation because ventricular depolarization occurs concurrently with ventricular repolarization.

Quinidine gluconate. Quinidine gluconate is a class IA drug that, because of its action on sodium channels, is effective in controlling a large variety of ventricular and supraventricular dysrhythmias. It is very effective in controlling ventricular tachycardia and can be administered as an infusion as a 0.64% solution administered at a rate of 1 L/hr/500 kg. Its cost makes it preferable to procainamide in the treatment of VT in the horse, although limited availability restricts its use. The drug is contraindicated in horses that are hypotensive as a result of the severity of their cardiac disease because it can cause peripheral vasodilation. Coadministration of quinidine gluconate with digoxin can result in higher than expected serum concentrations of both agents because of competitive protein binding.

Procainamide. Procainamide is also a class IA antidysrhythmic agent that does not have the vagolytic effects of quinidine and is less likely to induce hypotension. The drug can be administered intravenously and is the drug of choice for the treatment of ventricular tachycardia in the conscious horse. Unlike quinidine gluconate, no drug



Figure 11.4-7 Ambulatory electrocardiogram (ECG) from a 13-year-old pony gelding after exploratory celiotomy and enterotomy demonstrating multifocal ventricular tachycardia (VT1/VT2) with R-on-T phenomenon (VT3) which destabilized into ventricular fibrillation (VF) before death. Before this episode the ECG demonstrated several episodes of multifocal ventricular tachycardia and frequent isolated ventricular premature depolarizations; however, specific antidysrhythmic therapy was not instituted because of economic constraints and the presence of multiple concurrent noncardiac problems. IV procainamide would have been the drug of choice for the treatment of this case.

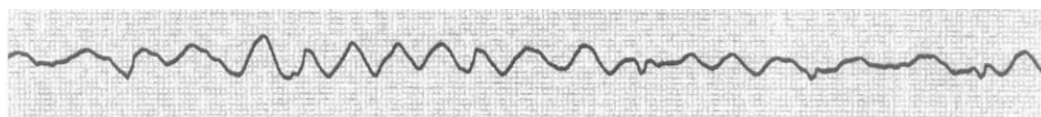


Figure 11.4-8 Base-apex electrocardiogram from a 16-year-old pony obtained during general anesthesia and exploratory celiotomy demonstrating coarse-wave ventricular fibrillation. Note the absence of atrial activity and wide ventricular complexes with no detectable T waves. This horse had received a large bolus (100 g) of potassium chloride as an IV bolus as a means of euthanasia. This treatment induced progressive atrial standstill, QRS prolongation, and ventricular fibrillation followed by asystole. Ventricular fibrillation lasted less than 1 minute.

interactions occur with digoxin; therefore procainamide is more suitable for use in horses with ventricular dysrhythmias and myocardial dysfunction.

Lidocaine. Lidocaine hydrochloride is a class IB antidysrhythmic agent that is the drug of choice to terminate ventricular tachydysrhythmias in anesthetized horses. However, because of the potential side effect of central nervous system excitement, care must be exercised when lidocaine is used in the conscious horse, in which excitement reactions can be seen after administration of bolus doses of 2 mg/kg. Lidocaine is most effective in the presence of a high extracellular concentration of potassium; therefore potassium supplementation may be considered in patients that are known or believed to be hypokalemic. Neurologic side effects can be controlled with the use of diazepam. Lidocaine can be administered as a bolus dose of 0.5 to 1 mg/kg and repeated every 5 to 10 minutes until conversion or until a total dose of 4 mg/kg is achieved. It can also be administered as a continuous infusion at a rate of 20 to 50 μ g/kg/min.

Magnesium sulfate. Magnesium sulfate is indicated for the treatment of ventricular dysrhythmias that are associated with hypomagnesemia and refractory dysrhythmias that are present even when serum magnesium levels are normal. Because magnesium is an ionized intracellular cation, accurate determination of hypomagnesemia is difficult, although ion-specific electrodes are becoming increasingly available on new blood-gas analyzers. Magnesium is primarily indicated for the treatment of *torsades des pointes*, a bizarre fluctuating ventricular tachycardia

that can be induced by several drugs, including quinidine (see Figure 11.4-7). The mechanism by which magnesium sulfate works in the hypomagnesemic state is in part related to the Na/K ATPase pump, for which magnesium is a cofactor, such that hypomagnesemia causes hypokalemia. In horses with normal serum magnesium concentrations, a calcium channel-blocking action is believed to account for its action. Magnesium can be administered in IV bolus doses of 4 mg/kg every 2 minutes to a total dose as high as 50 mg/kg.

Propranolol. Propranolol is a class II antidysrhythmic agent that slows the cardiac rate. Propranolol causes dose-dependent suppression of myocardial activity and as such is limited to the control of ventricular tachycardia, which is refractory to other antidysrhythmic therapy. This drug is especially useful for quinidine-induced dysrhythmias, because it has no effect on phase 1 of the cardiac action potential. Propranolol can only be administered by IV injection.

Ventricular Fibrillation

Ventricular fibrillation (VF) is usually a terminal dysrhythmia in horses and rarely persists long enough to require therapy. Electrocardiography demonstrates coarse or fine ventricular fibrillation waves as demonstrated in Figure 11.4-8. Successful treatment is limited to foals, where DC conversion is the method of choice. In the absence of DC conversion, bretylium has been advocated for treatment of VF in the foal. The mechanism of action is not fully understood, but has been shown to be superior to DC con-

version in human patients with refractory VF. Bretylium's use is limited to the foal because of its high cost.

Supplemental Readings

Reef VB: Arrhythmias. In Marr E (ed): *Cardiology of the Horse*, pp 177-209, London, WB Saunders, 1999.

Atrial Fibrillation

Bode F, Sachs F, Franz MR: Tarantula peptide inhibits atrial fibrillation. *Nature* 2001; 409:36.

Frye MA, Selders CG, Khursheed RM et al: Use of biphasic electrical conversion for treatment of idiopathic atrial fibrillation in two horses. *J Am Vet Med Assoc* 2002; 220:1039-1045.

Ohmura H, Hiraga A, Aida H et al: Determination of oral dosage and pharmacokinetic analysis of flecainide in horses. *J Vet Med Sci* 2001; 63:511-514.

Ohmura H, Nukada T, Mizuno Y et al: Safe and efficacious dosage of flecainide acetate for treating equine atrial fibrillation. *J Vet Med Sci* 2000; 62:711-715.

Muir WW, Reed SM, McGuirk SM: Treatment of atrial fibrillation in horses by intravenous administration of quinidine. *J Am Vet Med Assoc* 1999; 197:1607-1610.

Reef VB, Levitan CW, Spencer PA: Factors affecting prognosis and conversion in equine atrial fibrillation. *J Vet Intern Med* 1988; 2:1-6.

Reef VB, Reimer JM, Spencer PA: Treatment of atrial fibrillation in horses: new perspectives. *J Vet Intern Med* 1995; 9:57-67.

Ventricular Ectopy

Cornick JL, Seahorn TL: Cardiac arrhythmias identified in horses with duodenitis/proximal jejunitis: six cases (1985-1988). *J Am Vet Med Assoc* 1990; 197:1054-1059.

Marr CM, Reef VB, Brazil TJ et al: Aorto-cardiac fistulas in seven horses. *Vet Radiol Ultrasound* 1998; 39:22-31.

Reimer JM, Reef VB, Sweeney RW: Ventricular arrhythmias in horses: 21 cases (1984-1989). *J Am Vet Med Assoc* 1992; 201:1237-1243.

Wijnberg ID: Phenytoin sodium per os as a treatment for ventricular arrhythmia in the horse. Harrogate, UK, British Equine Veterinary Association Proceedings P218, 2001.

Wijnberg ID, van der Kolk JH, Hiddink EG: Use of phenytoin to treat digitalis-induced cardiac arrhythmias in a miniature Shetland pony. *Vet Rec* 1999; 144:259-261.

CHAPTER 11.5

Acquired Valvular Heart Disease

VIRGINIA B. REEF
Kennett Square, Pennsylvania

Valvular heart disease is more common in horses than previously recognized. Lesions on the aortic and mitral valve have been reported frequently in horses with murmurs of valvular regurgitation in both abattoir and echocardiographic studies. Tricuspid regurgitation has also frequently been reported in Standardbred racehorses and in National Hunt horses (horses that race over fences in the United Kingdom). Clinicians have difficulty differentiating physiologic flow murmurs from murmurs associated with valvular regurgitation because usually no clinical signs of cardiovascular disease are associated with the murmur. Careful characterization of the murmur can help the veterinarian differentiate physiologic flow murmurs from those of valvular insufficiency. A decision tree for horses with murmurs can be used to determine which horses need an echocardiogram and a more complete cardiac work-up (Boxes 11.5-1 and 11.5-2).

TRICUSPID REGURGITATION

Tricuspid insufficiency is the type of valvular regurgitation that is best tolerated in horses. Tricuspid regurgitation rarely affects a horse's performance or life expectancy, un-

less it is severe or significant right ventricular dysfunction is present. The murmur of tricuspid regurgitation is usually holosystolic or pansystolic and band shaped, with its point of maximal intensity on the right side of the chest, usually in the fourth intercostal space. Occasionally the murmur is soft and blowing or crescendo in quality. The crescendo murmurs are most consistent with tricuspid valve prolapse and are infrequently detected in horses. Murmurs of tricuspid prolapse may be shorter in duration, detected primarily in mid to late systole. Musical murmurs are usually associated with a portion of the valve or chordal apparatus vibrating within the heart and are more frequently found in horses with a ruptured chorda tendineae. The louder the murmur of tricuspid regurgitation and the longer its duration, the larger the regurgitant jet that is detected with color-flow Doppler echocardiography. Clinically significant tricuspid regurgitation murmurs are usually a grade 3 out of 6 or greater.

The detection of a grade 3 out of 6 or louder right-sided systolic murmur in a horse with atrial fibrillation indicates probable tricuspid regurgitation and right atrial enlargement. Echocardiographic examination is indicated in these horses to determine the degree of atrial enlargement

version in human patients with refractory VF. Bretylium's use is limited to the foal because of its high cost.

Supplemental Readings

Reef VB: Arrhythmias. In Marr E (ed): *Cardiology of the Horse*, pp 177-209, London, WB Saunders, 1999.

Atrial Fibrillation

Bode F, Sachs F, Franz MR: Tarantula peptide inhibits atrial fibrillation. *Nature* 2001; 409:36.

Frye MA, Selders CG, Khursheed RM et al: Use of biphasic electrical conversion for treatment of idiopathic atrial fibrillation in two horses. *J Am Vet Med Assoc* 2002; 220:1039-1045.

Ohmura H, Hiraga A, Aida H et al: Determination of oral dosage and pharmacokinetic analysis of flecainide in horses. *J Vet Med Sci* 2001; 63:511-514.

Ohmura H, Nukada T, Mizuno Y et al: Safe and efficacious dosage of flecainide acetate for treating equine atrial fibrillation. *J Vet Med Sci* 2000; 62:711-715.

Muir WW, Reed SM, McGuirk SM: Treatment of atrial fibrillation in horses by intravenous administration of quinidine. *J Am Vet Med Assoc* 1999; 197:1607-1610.

Reef VB, Levitan CW, Spencer PA: Factors affecting prognosis and conversion in equine atrial fibrillation. *J Vet Intern Med* 1988; 2:1-6.

Reef VB, Reimer JM, Spencer PA: Treatment of atrial fibrillation in horses: new perspectives. *J Vet Intern Med* 1995; 9:57-67.

Ventricular Ectopy

Cornick JL, Seahorn TL: Cardiac arrhythmias identified in horses with duodenitis/proximal jejunitis: six cases (1985-1988). *J Am Vet Med Assoc* 1990; 197:1054-1059.

Marr CM, Reef VB, Brazil TJ et al: Aorto-cardiac fistulas in seven horses. *Vet Radiol Ultrasound* 1998; 39:22-31.

Reimer JM, Reef VB, Sweeney RW: Ventricular arrhythmias in horses: 21 cases (1984-1989). *J Am Vet Med Assoc* 1992; 201:1237-1243.

Wijnberg ID: Phenytoin sodium per os as a treatment for ventricular arrhythmia in the horse. Harrogate, UK, British Equine Veterinary Association Proceedings P218, 2001.

Wijnberg ID, van der Kolk JH, Hiddink EG: Use of phenytoin to treat digitalis-induced cardiac arrhythmias in a miniature Shetland pony. *Vet Rec* 1999; 144:259-261.

CHAPTER 11.5

Acquired Valvular Heart Disease

VIRGINIA B. REEF
Kennett Square, Pennsylvania

Valvular heart disease is more common in horses than previously recognized. Lesions on the aortic and mitral valve have been reported frequently in horses with murmurs of valvular regurgitation in both abattoir and echocardiographic studies. Tricuspid regurgitation has also frequently been reported in Standardbred racehorses and in National Hunt horses (horses that race over fences in the United Kingdom). Clinicians have difficulty differentiating physiologic flow murmurs from murmurs associated with valvular regurgitation because usually no clinical signs of cardiovascular disease are associated with the murmur. Careful characterization of the murmur can help the veterinarian differentiate physiologic flow murmurs from those of valvular insufficiency. A decision tree for horses with murmurs can be used to determine which horses need an echocardiogram and a more complete cardiac work-up (Boxes 11.5-1 and 11.5-2).

TRICUSPID REGURGITATION

Tricuspid insufficiency is the type of valvular regurgitation that is best tolerated in horses. Tricuspid regurgitation rarely affects a horse's performance or life expectancy, un-

less it is severe or significant right ventricular dysfunction is present. The murmur of tricuspid regurgitation is usually holosystolic or pansystolic and band shaped, with its point of maximal intensity on the right side of the chest, usually in the fourth intercostal space. Occasionally the murmur is soft and blowing or crescendo in quality. The crescendo murmurs are most consistent with tricuspid valve prolapse and are infrequently detected in horses. Murmurs of tricuspid prolapse may be shorter in duration, detected primarily in mid to late systole. Musical murmurs are usually associated with a portion of the valve or chordal apparatus vibrating within the heart and are more frequently found in horses with a ruptured chorda tendineae. The louder the murmur of tricuspid regurgitation and the longer its duration, the larger the regurgitant jet that is detected with color-flow Doppler echocardiography. Clinically significant tricuspid regurgitation murmurs are usually a grade 3 out of 6 or greater.

The detection of a grade 3 out of 6 or louder right-sided systolic murmur in a horse with atrial fibrillation indicates probable tricuspid regurgitation and right atrial enlargement. Echocardiographic examination is indicated in these horses to determine the degree of atrial enlargement

BOX 11.5-1**Indications for an Echocardiogram in Horses with Systolic Murmurs****Right-Sided Murmur**

Murmur of pulmonic stenosis
 Murmur of mitral regurgitation
 Atrial fibrillation
 Grade 4 to 6 out of 6 holosystolic or pansystolic murmur
 Signs of cardiovascular disease
 Poor performance or exercise intolerance

Left-Sided Murmur

Band-shaped murmur
 Signs of pulmonary compromise
 Atrial fibrillation
 Grade 4 to 6 of 6 holosystolic or pansystolic murmur
 Signs of cardiovascular disease
 Poor performance or exercise intolerance

BOX 11.5-2**Indications for an Echocardiogram in Horses with Diastolic or Continuous Murmurs**

Diastolic murmur associated with any of the following:

- Atrial fibrillation
- Ventricular premature contractions
- Murmur of mitral regurgitation
- Murmur of ventricular septal defect
- Bounding pulses
- Signs of cardiovascular disease
- Poor performance or exercise intolerance

Continuous murmur:

- Always unless less than 4 days' duration

before an attempt at conversion to sinus rhythm (see Box 11.5-1). Atrial enlargement slightly decreases the prognosis for successful conversion and increases the likelihood that the horse will experience a recurrence of atrial fibrillation. Lesions are less frequently detected on the tricuspid valve in horses with tricuspid regurgitation than on the mitral valve in horses with mitral regurgitation. Many horses with murmurs of tricuspid regurgitation have normally appearing tricuspid valves with a normal size right atrium and ventricle. Thickening of the tricuspid valve leaflets, tricuspid valve prolapse, ruptured chordae tendineae or a flail tricuspid leaflet (Figure 11.5-1) are occasionally detected echocardiographically. Endocarditis lesions that involve the tricuspid valve are uncommon. Most horses with tricuspid endocarditis have concurrent septic jugular vein thrombophlebitis.

Enlargement of the right atrium is subjective and best evaluated in the right parasternal, four-chamber view where it can be compared with the left atrium. The two atria should be similar in size, and the clinician should

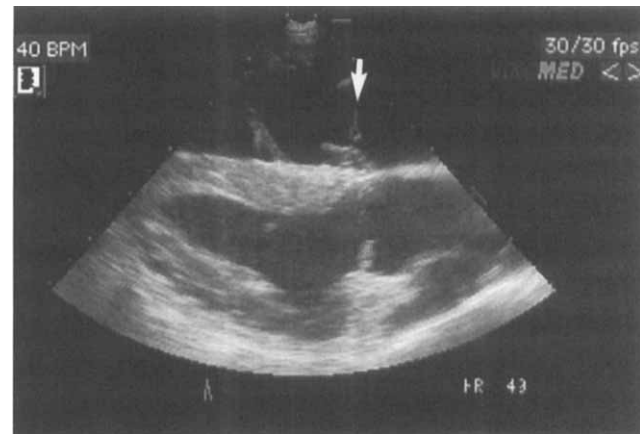


Figure 11.5-1 Two-dimensional echocardiogram of a horse with a flail cranial tricuspid valve leaflet and severe tricuspid regurgitation. Notice the cranial leaflet of the tricuspid valve everting into the right atrium in this diastolic frame (arrow). The cranial leaflet of the tricuspid valve is pointing towards the right free wall. Present are right atrial and right ventricular enlargement and a prominent moderator band in the right ventricle.

take into account the fact that the entire right atrium cannot be imaged because it is close to the chest wall and the angle of the field of view is not large enough to include it in its entirety. The right ventricle should also be compared to the left ventricle in this view and should be approximately one half to one third of the diameter of the left ventricle in the parasternal long-axis, four-chamber view. Paradoxical motion of the interventricular septum (movement of the interventricular septum towards the right ventricle in systole instead of towards the left ventricle) indicates significant right ventricular volume overload and moderate-to-severe tricuspid regurgitation (Figure 11.5-2).

Tricuspid regurgitation may be primary, associated with the aforementioned abnormalities of the tricuspid valve, or may develop secondary to significant left-sided valvular heart disease. Tricuspid regurgitation also commonly develops in horses with cardiomyopathy. Most horses with clinical signs of right-sided congestive heart failure have the primary pathology on the aortic and/or mitral valves and are also in left-sided congestive heart failure. The left-sided congestive heart failure leads to the development of pulmonary hypertension and right-sided heart failure. The clinical signs of left-sided congestive heart failure are usually subtle and are often missed. The increased resting respiratory rate, occasional cough, and exercise intolerance are often attributed to primary pulmonary disease. It is not until the horse develops ventral edema, in many cases, that the heart is evaluated more critically. A careful clinical and echocardiographic examination is indicated in all horses presenting with right-sided congestive heart failure and systolic murmurs audible on both sides of the chest, to determine the reason for the development of congestive heart failure.

Marked generalized venous distention, jugular pulsations, and ventral edema are clinical signs of right-sided

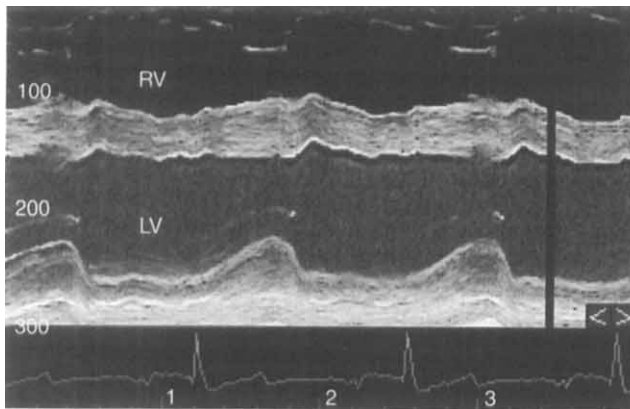


Figure 11.5-2 M-mode echocardiogram of both ventricles from the horse in Figure 11.5-1 demonstrating paradoxical septal motion. Notice the movement of the interventricular septum toward the right ventricle (RV) in systole, instead of toward the left ventricle (LV).

congestive heart failure. The edema often begins in the prepuce or as a small plaque along the ventral-most portion of the abdomen and progresses to pectoral edema and generalized ventral edema. Limb edema is usually only detected in horses with advanced right-sided congestive heart failure. Stocking up of the extremities, in the absence of ventral edema and generalized venous distention, is not an indication of cardiovascular disease. Supportive treatment with diuretics, positive inotropic drugs, and vasodilators is indicated, but usually only results in a temporary (2-6 month) improvement until the clinical signs of congestive heart failure return because of the advanced underlying myocardial and/or valvular heart disease.

MITRAL REGURGITATION

Mitral insufficiency is the type of valvular insufficiency that is most likely to affect performance and shorten life expectancy. Mitral regurgitation murmurs are found in horses of all ages and breeds. Mitral regurgitation murmurs are also usually holosystolic or pansystolic and band shaped but have their point of maximal intensity in the mitral to aortic valve region. These murmurs usually radiate dorsally and can often be heard over the midthorax in the left fifth to seventh intercostal spaces. Crescendo mid to late systolic murmurs are typical of mitral valve prolapse. Murmurs of mitral valve prolapse occasionally are holosystolic, usually in horses with larger jets of mitral regurgitation. Honking musical murmurs are found in horses with a ruptured chorda tendineae. The intensity of the murmur of mitral regurgitation does not correlate with its severity. Any loud systolic murmur ausculted on the left side of the horse's thorax should be considered to be mitral regurgitation, until proven otherwise.

Atrial fibrillation is common in horses with moderate-to-severe mitral regurgitation and left atrial enlargement. Detection of supraventricular premature depolarizations may precede the development of atrial fibrillation in horses with atrial enlargement. Although atrial tachycardia has been occasionally detected in horses with moder-

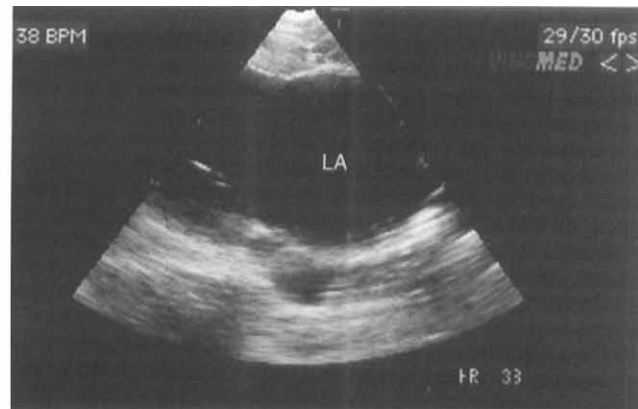


Figure 11.5-3 Left parasternal two-dimensional echocardiogram of the left atrium, mitral valve, and left ventricle in a horse with left-sided congestive heart failure from severe mitral regurgitation. Notice the rounded appearance of the left atrium (LA) indicating increased left atrial pressures.

ate-to-severe mitral regurgitation and may precede the development of atrial fibrillation in these horses, it is an uncommon arrhythmia.

Clinical Signs

Clinical signs in horses with mitral regurgitation are usually associated with the respiratory system and are often so subtle that they are mistaken for primary respiratory disease or missed altogether. Coughing, flared nostrils, labored breathing, exercise intolerance, prolonged recovery after exercise, and an elevated resting respiratory rate are the most common clinical signs. The coughing is usually only occasional and often occurs at rest and during exercise. Fulminant pulmonary edema with the expectoration of foamy fluid is infrequently present in horses with primary mitral valve disease, unless they have experienced rupture of a major chorda tendineae. Many horses are presented to the veterinarian once they have developed clinical signs of right-sided heart failure. Careful questioning usually reveals a period of weeks to a month or more in which the horse exhibited some of the aforementioned respiratory signs.

Diagnosis

Echocardiographic examination is indicated for horses with grade 3 to 6 out of 6 holosystolic or pansystolic murmurs with their point of maximal intensity in the mitral or aortic valve area (see Box 11.5-1). A wide variation exists in normal left ventricular end diastolic diameters within the various breeds of horses. Similar variation exists in the maximal diameter of the left atrium when measured from the left parasternal window between different horses. In this view, the maximal left atrial diameter in all light breeds of horses should not exceed 13.5 cm. When viewed from the right parasternal window, the two atria should appear similar in size. A turgid appearance of the left atrium is an indication of increased left atrial pressure (Figure 11.5-3). The interatrial septum should divide the atria

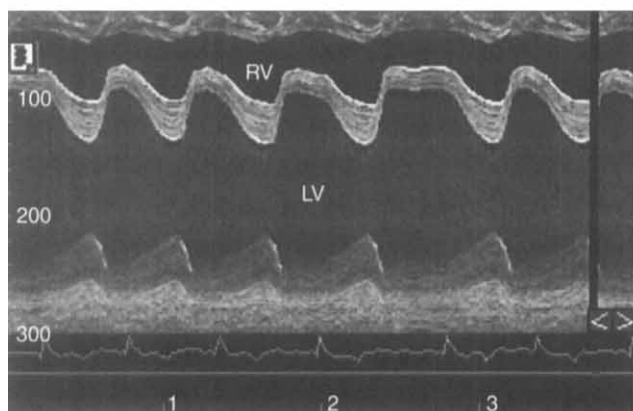


Figure 11.5-4 M-mode echocardiogram of both ventricles obtained from a horse with congestive heart failure and severe mitral regurgitation. Notice the swinging pattern of motion of the interventricular septum, the markedly dilated left ventricle (LV) and the less vigorously moving left ventricular free wall. This horse had a fractional shortening of 32%. RV, Right ventricle.



Figure 11.5-5 Two-dimensional echocardiogram of a prolapsing accessory leaflet of the mitral valve obtained from the left parasternal long-axis view of the mitral valve. Notice the bulging of the leaflet (arrow) into the left atrium. Present are left atrial and left ventricular enlargement with some rounding of the left atrium apparent.

into two relatively equal chambers and should not bulge towards the right or left side. Bulging of the interatrial septum is an indication of increased pressures within the chamber on the concave side of the bulge. Increased left ventricular end diastolic diameter with thinning of the left ventricular free wall and interventricular septum indicates left ventricular volume overload. An increase in the fractional shortening is the normal response to a volume overloaded left ventricle and should be present in horses with normal left ventricular myocardial function. Myocardial dysfunction is present if the fractional shortening is normal in horses with moderate-to-severe mitral regurgitation and an enlarged left ventricle (Figure 11.5-4).

Bulging of all or part of one of the mitral valve leaflets into the left atrium during systole is consistent with mitral valve prolapse (Figure 11.5-5). Often it is one of the acces-



Figure 11.5-6 Two-dimensional echocardiogram obtained from a horse with a ruptured chordae tendineae and mitral regurgitation. Notice the thin chordal structure everting into the left atrium in systole (arrow). Present are both left atrial and left ventricular enlargement.

sory leaflets of the mitral valve that is prolapsing into the left atrium. Prolapse of one of the accessory mitral valve leaflets is best imaged from the left parasternal long-axis view of the mitral valve, because these leaflets are not usually imaged from the right parasternal window. Ruptured chordae tendineae also more frequently involve the accessory leaflets and thus are best imaged from the left parasternal long-axis window (Figure 11.5-6). The ruptured chorda tendineae is imaged everting into the left atrium in systole or diastole and moves asynchronously with the rest of the mitral valve. The mitral valve leaflets should be carefully evaluated from both parasternal windows for thickening, prolapse, a flail leaflet, a vegetative lesion, or ruptured chordae tendineae.

Pulsed-wave and color-flow Doppler echocardiographic examination of the mitral valve and left atrium should be performed from both parasternal windows. The best studies, however, are usually obtained from the left parasternal window, because the mitral valve and left atrium are closer to the transducer. The size of the regurgitant jet should be mapped with pulsed-wave or color-flow Doppler echocardiography to estimate the severity of the mitral regurgitation. A jet that occupies a large portion of the atria with a normal to near normal left atrial diameter is consistent with acute onset moderate to severe mitral regurgitation. Left atrial diameter should be measured in the left parasternal, two-chamber view in all horses with murmurs of mitral regurgitation, aortic regurgitation, and atrial fibrillation, to more objectively evaluate left atrial size. Congestive heart failure can develop in horses with severe acute mitral regurgitation when the left atrial diameter is 16 cm in diameter, or in horses with long standing, slowly progressive mitral regurgitation when the left atrial diameter is greater than 22 cm. These horses usually present in atrial fibrillation caused by the atrial enlargement, but if mitral regurgitation is acute and severe, atrial premature depolarizations or atrial tachycardia may be present.

Horses with a markedly turgid, enlarged left atrium and pulmonary hypertension are not safe to ride because of the risk of sudden death from atrial or pulmonary artery

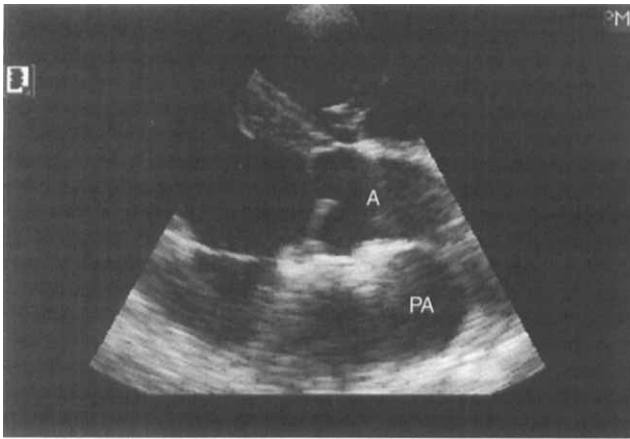


Figure 11.5-7 Two-dimensional echocardiogram of a horse with pulmonary hypertension from severe mitral regurgitation. Notice the rounded main pulmonary artery (PA) that is larger than the root of the aorta (A) consistent with pulmonary hypertension. Compare the pulmonary artery diameter here to that from the horse in Figure 11.5-8 with normal pulmonary arterial pressures.

rupture. The diameter of the aorta and pulmonary artery should be measured at the same location relative to the valve leaflets in all horses with significant mitral regurgitation. A pulmonary artery diameter in excess of the aortic diameter is indicative of pulmonary hypertension (Figure 11.5-7). If the pulmonary artery measures 1 cm larger in diameter than the aorta, this usually indicates systemic pressures in the pulmonary circulation (approximately 100 mm Hg).

Pulsed-wave Doppler or color-flow Doppler echocardiographic evaluation of the regurgitant jet is important to assess the severity and chronicity of the mitral regurgitation. However, underestimation of the size of the regurgitant jet in horses is common, because the angles for interrogation of the regurgitant jet are often perpendicular to the transducer, not parallel. With Doppler echocardiography, no flow is detectable if the regurgitant jet is 90 degrees to the ultrasound beam. The pulsed-wave and color-flow Doppler echocardiographic examination should be performed by using views that will maximize the ability to detect abnormal flow, rather than by using the views that are ideal for M-mode and two-dimensional imaging.

Horses with mild mitral regurgitation and mitral valve prolapse have an excellent prognosis for performance and usually have a normal life expectancy. Similarly, if the amount of mitral regurgitation is small and the mitral valve leaflets appear normal or only slightly thickened, the horse should also do well. Moderate-to-severe thickening of the mitral valve leaflets is usually associated with the development of jets of mitral regurgitation that gradually increase in size and may affect the performance of the horse or its life expectancy. Less extensive ruptures of the chordae tendineae or bacterial endocarditis usually results in the more rapid development of significant valvular insufficiency with the probability that the horse's performance will be affected with subsequent shortening of the horse's life expectancy. The rupture of a major chorda tendineae of the mitral valve usually results in the horse developing acute pulmonary edema and respiratory dis-

tress associated with the acute onset of left-sided congestive heart failure.

Treatment

Treatment for congestive heart failure is usually supportive with the majority of horses responding to treatment. Clinical improvement is usually short lived, however, lasting only 2 to 6 months. Diuretics, vasodilators, and positive inotropic drugs are the mainstay of treatment for congestive heart failure. Furosemide is usually administered orally as needed with a maintenance dose of 0.5 to 1 mg/kg orally twice daily. Digoxin (0.011 mg/kg PO) and enalapril (0.5 mg/kg PO) are usually administered orally twice daily. Blood should be obtained for creatinine and electrolyte determinations before beginning treatment for congestive heart failure. Digoxin should be used with care in horses with azotemia as digoxin toxicity is more likely to develop in these horses. Any electrolyte abnormalities should be corrected because these may predispose the horse to the development of other arrhythmias. A peak and trough digoxin concentration should be determined in all horses 5 to 7 days after initiating treatment to be sure that the horse's digoxin concentration is maintained in the therapeutic range (1-2 ng/ml). Potassium supplementation is occasionally needed in horses being treated long term for congestive heart failure.

AORTIC REGURGITATION

Aortic regurgitation is most commonly found in older horses, although horses of any age may develop this disease. Degenerative changes in the aortic leaflets have been reported in abattoir studies and are most common in aged horses in normal sinus rhythm. The most common degenerative valve changes reported are fibrous band lesions parallel to the free edge of the leaflet and nodular thickening of the free edge of the aortic cusp.

Ventricular premature depolarizations have been reported to occur more frequently in horses with murmurs of aortic regurgitation. Paroxysms of ventricular tachycardia and multiform ventricular arrhythmias have been detected in horses with aortic regurgitation and may be a negative prognostic indicator. In a large study in the United Kingdom, these horses were more likely to have died or to have been humanely destroyed 2 years after the detection of the aortic regurgitation murmur when compared with horses with aortic regurgitation that did not have demonstrable ventricular ectopy. The pathophysiology of the ventricular premature depolarizations is unclear. The ventricular premature depolarizations may occur secondary to decreased myocardial perfusion in horses with severe aortic regurgitation, may be related to the increased sympathetic tone associated with the development of left-sided congestive heart failure, or may be secondary to concurrent myocardial disease in older horses. The development of ventricular premature depolarizations may be an indication of more severe aortic regurgitation, but this association has yet to be proven. Atrial fibrillation also occurs in horses with chronic, moderate-to-severe aortic regurgitation. Left atrial enlargement often develops in these horses associated with chronic left ventricular enlargement, predisposing these horses to atrial fibrillation.

Clinical Signs

Any holodiastolic murmur detected in a horse should be considered to be caused by insufficiency of the aortic valve until proven otherwise. The most common murmur of aortic regurgitation is a holodiastolic decrescendo murmur, although musical holodiastolic decrescendo murmurs are also frequently detected. The murmur is usually loudest in the aortic valve area, radiating to the mitral valve area and left and right apex. The musical component of the murmur indicates that some portion of the aortic valve is vibrating during diastole. The vibrating portion of the valve may be a redundant leaflet, a fenestration, or a tear of the free edge of the valve leaflet. No correlation has been made between the intensity of the murmur of aortic regurgitation and its severity, although louder aortic regurgitation murmurs have been associated with a poorer outcome in horses in the United Kingdom. The arterial pulses become bounding with the development of a left ventricular volume overload and are a good indication of the severity of aortic regurgitation. Diastolic pressures of less than 60 mm Hg are an indication of significant run off from the aorta into the left ventricle in diastole.

Diagnosis

Resting 24-hour continuous electrocardiograms obtained with a Holter monitor and exercising electrocardiograms are recommended for horses with moderate-to-severe aortic regurgitation, to determine if ventricular premature depolarizations are present at rest or during exercise, to determine the severity of the arrhythmias detected, and to determine whether or not the horse is safe to continue to use for performance. Occasional ventricular premature depolarizations (VPDs) are detected during routine continuous electrocardiography in clinically normal horses, but they should be uniform and occur at a frequency of less than 1 per hour. More frequent ventricular premature depolarizations, multiform ventricular premature depolarizations, pairs of VPDs, or paroxysms of ventricular tachycardia should not be detected. Ventricular premature depolarizations should not be detected during exercise but occasional VPDs are present in some horses in the immediate post exercise period, most likely associated with autonomic imbalance at this time.

An echocardiogram is indicated in all horses with holodiastolic murmurs and bounding arterial pulses, because these horses have aortic regurgitation with a left ventricular volume overload. The echocardiogram will help to determine the severity of the left ventricular volume overload, the valvular pathology that is present and how the myocardium is coping with the increased volume load. Marked increases in the left ventricular internal diameter at end diastole and in the fractional shortening are present in horses with moderate to severe aortic regurgitation and normal myocardial function. As with mitral regurgitation, a normal (or decreased) shortening fraction is an indication of impending myocardial failure in horses with large left ventricular end diastolic diameters and large jets detected with pulsed-wave or color-flow Doppler echocardiography. Thickening of the left coronary leaflet of the aortic valve is usually parallel to the free edge (Figure 11.5-8) or appears as a nodule on the free edge of the leaflet. Fenestrations of the aortic leaflet can



Figure 11.5-8 Thickening of the left coronary leaflet of the aortic valve (*arrow*) in an older horse (24 years) with chronic aortic regurgitation of moderate severity. Notice the increase in the echogenicity and thickness of the aortic leaflet parallel to the free edge.

also be imaged and usually involve the left coronary leaflet of the aortic valve. Tears in the free edge of the leaflet are uncommon and usually result in acute severe aortic regurgitation if they occur. Bacterial endocarditis lesions occasionally involve the aortic leaflets or, less commonly, the aortic root. Aortic regurgitation usually results in high-frequency vibrations of the septal leaflet of the mitral valve in diastole as it moves into the left ventricular outflow track. Less frequently, high-frequency vibrations can be imaged on the left ventricular side of the interventricular septum when the jet is directed towards the septum. The size of the jet at its origin and the size of the jet in the left ventricular outflow track, determined with pulsed-wave or color-flow Doppler echocardiography, and the slope of the regurgitant jet (pressure half time) determined with continuous wave Doppler echocardiography are all indicators of the severity of the aortic regurgitation (Figure 11.5-9). A short pressure half time is associated with a rapid increase in left ventricular pressure in diastole and more severe aortic regurgitation.

Treatment

Horses with moderate-or-severe aortic regurgitation may benefit from the use of angiotensin-converting enzyme (ACE) inhibitors, such as enalapril, in hopes of prolonging their useful performance life. Although conflicting reports exist in the veterinary and human literature as to the efficacy of ACE inhibition in prolonging life expectancy, this class of drugs appears to be beneficial in prolonging the useful performance life of horses with moderate-to-severe aortic regurgitation. Treatment for congestive heart failure can also be initiated in horses with severe aortic regurgitation and left-sided congestive heart failure, as for horses with mitral and/or tricuspid regurgitation, but usually only results in temporary improvement.

Most horses with aortic regurgitation have a favorable prognosis for performance and life, as the aortic regurgitation is often mild at the onset, progresses slowly, and infrequently results in the horse developing congestive heart failure. Although the study in the United Kingdom did

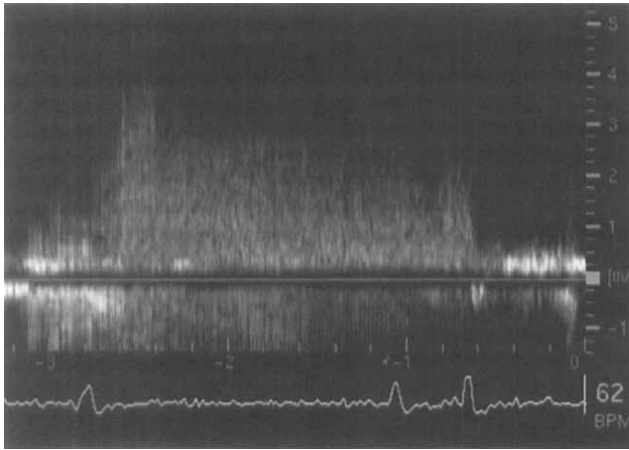


Figure 11.5-9 Continuous-wave Doppler tracing of the aortic regurgitation jet demonstrates a moderate slope of the regurgitant blood flow back into the left ventricle during diastole associated with aortic regurgitation of moderate severity.

demonstrate a decreased survival in horses diagnosed with aortic regurgitation compared with those without, it is not clear if this was caused by cardiovascular disease. Additional studies are needed to determine the cause of death in horses with aortic regurgitation and if their normal life expectancy is reached in most instances. Horses with moderate-to-severe aortic regurgitation should be evaluated electrocardiographically, both at rest over a 24-hour period and during exercise, to be sure that they are safe to ride.

PULMONIC REGURGITATION

Pulmonic regurgitation in horses is rare as an isolated or primary valvular insufficiency. Pulmonic regurgitation is most frequently detected in horses with long-standing pulmonary hypertension associated with left-sided congestive heart failure. Pulmonic regurgitation is usually present in horses with biventricular failure associated with severe aortic and/or mitral regurgitation.

Clinical Signs and Diagnosis

Although clinically insignificant to mild amounts of pulmonic regurgitation are frequently detected with color-flow Doppler echocardiography, pulmonic regurgitation murmurs are rarely audible. Clinically insignificant or mild pulmonic regurgitation is frequently detected in clinically normal horses, as well as in horses with valvular heart disease or in horses with ventricular septal defects. Horses with moderately-sized ventricular septal defects and a normal life expectancy often develop pulmonic insufficiency after many years because of the pulmonary overcirculation and stretching of the pulmonary artery that occurs with long-standing pulmonary overcirculation. Although pulmonic insufficiency should be kept on the differential diagnosis list for horses with holodiastolic decrescendo murmurs, horses with a holodiastolic decrescendo murmur should be considered to have aortic insufficiency until proven otherwise. The paucity of audible holodiastolic murmurs of pulmonic regurgitation can be attributed to

the small pressure difference in diastole normally present between the pulmonary artery and right ventricle.

Supplemental Readings

- Bishop SP, Cole C, Smetzer DL: Functional and morphologic pathology of equine aortic insufficiency. *Path Vet* 1996; 3:137-158.
- Blissitt KJ: Auscultation. In Marr CM (ed): *Cardiology of the Horse*, pp 73-92, London, WB Saunders, 1999.
- Blissitt KJ, Bonagura JD: Colour flow Doppler echocardiography in horses with cardiac murmurs. *Equine Vet J Suppl* 1995; 19:82-85.
- Bonagura JD: Clinical evaluation and management of heart disease. *Equine Vet Educ* 1990; 2:31-37.
- Collatos C, Clark ES, Reef VB et al: Atrial fibrillation, cardiomegaly, left atrial mass and *Rhodococcus equi* septic osteoarthritis in a Thoroughbred colt. *J Am Vet Med Assoc* 1990; 197:1039-1042.
- Davis JL, Gardner SY, Schwabenton B et al: Congestive heart failure in horses: 14 cases (1984-2001). *J Am Vet Med Assoc* 2002; 220:1512-1515.
- Dedrick P, Reef VB, Sweeney RW et al: Treatment of bacterial endocarditis in a horse. *J Am Vet Med Assoc* 1988; 193:339-342.
- Hillyer MH, Mair TS, Holmes JR: Treatment of bacterial endocarditis in a Shire mare. *Equine Vet Educ* 1990; 2:5-7.
- Kriz NG, Hodgson DR, Rose RJ: Prevalence and clinical importance of heart murmurs in racehorses. *J Am Vet Med Assoc* 2000; 216:1441-1445.
- Marr CM, Pirie HM, Northridge DB: Confirmation by Doppler echocardiography of valvular regurgitation in a horse with a ruptured chorda tendinea of the mitral valve. *Vet Rec* 1990; 27:376-379.
- Marr CM, Reef VB: Physiological valvular regurgitation in clinically normal young racehorses: prevalence and two-dimensional characteristics. *Equine Vet J Suppl* 1995; 19:56-62.
- Maxson AD, Reef VB: Bacterial endocarditis in horses: ten cases (1984-1995). *Equine Vet J* 1997; 29:394-399.
- Nilsfors L, Lombard CW, Weckner D et al: Diagnosis of pulmonic valve endocarditis in a horse. *Equine Vet J* 1991; 23:479-482.
- Patteson MW, Cripps PJ: A survey of cardiac auscultatory findings in horses. *Equine Vet J* 1993; 25:409-415.
- Reef VB: Cardiovascular ultrasonography. In Reef VB (ed): *Equine Diagnostic Ultrasound*, pp 215-272, Philadelphia, WB Saunders, 1998.
- Reef VB: Echocardiographic examination in the horse: the basics. *Comp Cont Educ Pract Vet* 1990; 12:1312-1320.
- Reef VB: Evaluation of the equine cardiovascular system. *Vet Clin N Am Equine Pract* 1985; 1:275-288.
- Reef VB: Heart murmurs in horses: determining their significance with echocardiography. *Equine Vet J Suppl* 1995; 19:71-80.
- Reef VB: Mitral valvular insufficiency associated with ruptured chordae tendineae in three foals. *J Am Vet Med Assoc* 1987; 191:329-331.
- Reef VB, Bain FT, Spencer PA: Severe mitral regurgitation in horses: clinical, echocardiographic, and pathologic findings. *Equine Vet J* 1998; 30:18-27.
- Reef VB, Reimer JM, Spencer PA: Treatment of equine atrial fibrillation: new perspectives. *J Vet Intern Med* 1995; 9:57-67.
- Reef VB, Spencer P: Echocardiographic evaluation of equine aortic insufficiency. *Am J Vet Res* 1987; 48:904-909.
- Reimer J, Reef VB: Echocardiographic detection of pulmonic valve rupture in a horse with right-sided failure. *J Am Vet Med Assoc* 1991; 198:880-882.

CHAPTER 11.6

Myocardial Disease

MEG M. SLEEPER

Philadelphia, Pennsylvania

Myocarditis is an inflammatory process that involves the myocardial wall. It usually is caused by bacterial or viral infections but also can be due to parasite infestation and the associated thromboembolic events. *Staphylococcus aureus*, *Streptococcus equi*, *Clostridium chauvoei*, and *Mycobacterium* sp. have been associated with equine myocardial disease in the past. Known viral causes include equine infectious anemia, equine viral arteritis, and equine influenza. Parasitic etiologies include strongylosis or onchocerciasis. Myocarditis also can occur after pericarditis, endocarditis, allergic reactions and secondary to pharmacologic agents.

Cardiomyopathy is a subacute or chronic disease of the myocardium that occurs without anatomic valvular disease, congenital cardiac malformation, or pulmonary disease. Dilated cardiomyopathy is the primary form of cardiomyopathy in the horse, and the most common cause is probably myocarditis. Toxic insult also can result in dilated cardiomyopathy. Acute monensin intoxication results in decreased systolic function with a normal heart size; however, eventually the cardiac changes are similar to idiopathic dilated cardiomyopathy. These signs include ventricular dilation, increased ventricular mass, and decreased systolic function. Although rare, intoxication by ingestion of lasalocid, salinomycin, and heavy metals also has been incriminated as a cause of dilated cardiomyopathy. Other less common causes include neoplastic infiltration, hypoxic or ischemic insults, and nutritional deficiencies such as lack of vitamin E, selenium, or copper. A fibroadipose form of cardiomyopathy also has been recognized in the horse. However, because the etiology often is undetermined, most cases of dilated cardiomyopathy are labeled idiopathic.

As dilated cardiomyopathy progresses, several changes occur in an attempt to compensate for reduced cardiac output, which is secondary to the primary myocardial dysfunction. The heart size increases; circulating blood volume increases through activation of the renin-angiotensin-aldosterone system; and arterial resistance increases. These compensatory mechanisms are helpful in the short term, but ultimately, the increased cardiac preload and afterload result in further reduction of cardiac output and signs of congestive heart failure may develop.

CLINICAL SIGNS

Clinical signs are variable depending on the extent of the disease and associated systemic illness. Myocarditis frequently can be difficult to distinguish from colic, respiratory disease, or lameness because of vague signs. The first indication of disease may be poor performance or sudden

death, or the diagnosis may be an incidental finding. Fever may be present. Clinical signs of cardiomyopathy often are associated more clearly with cardiovascular disease. Exercise intolerance is common, and affected animals often have elevated heart rates during exercise and prolonged recovery from exercise. A resting sinus tachycardia or other dysrhythmias may be heard; however, the resting heart rate also may be normal. Systolic murmurs and/or pronounced gallop rhythms may be present. If congestive heart failure develops, jugular distention, jugular pulses, subcutaneous edema, respiratory distress, or circulatory collapse is also likely.

LABORATORY FINDINGS

Clinical pathology findings are often nonspecific. Liver enzymes may be elevated because of passive congestion. Markers of myocardial damage such as cardiac isoenzymes of creatine kinase (CKMB), lactate dehydrogenase (LDH), and α -hydroxybutyrate dehydrogenase (HBDH) and/or cardiac troponin-I may be elevated. Large elevations of CKMB and HBDH have been detected in a monensin toxicity outbreak and have been detected in other horses with myocardial necrosis of unknown cause. Serum also should be evaluated for evidence of viral infection (particularly influenza, equine viral arteritis, equine infectious anemia, and herpesvirus). Hemoglobinuria, if present, suggests that monensin, gossypol, or nutritional myodegeneration is a more likely cause.

Changes in the electrocardiogram (ECG) are nonspecific and include sinus tachycardia or dysrhythmias. Echocardiography may be normal in cases of myocarditis, or abnormalities may be secondary to dysrhythmias. However, with both severe myocarditis and dilated cardiomyopathy, there is increased ventricular chamber size during both systole and diastole, decreased thickness of the left ventricular walls, and decreased systolic function. The latter is evidenced by a reduction of the shortening fraction, ejection fraction, and total or regional myocardial dyskinesis or akinesis (Figure 11.6-1). The left atrium may be enlarged, and the E point to septal separation often is increased because of left ventricular dilation and decreased cardiac output. E point to septal separation is the distance between the maximal opening of the septal leaflet of the mitral valve and the interventricular septum. The aorta may be decreased in size because of a reduction in cardiac output, and the pulmonary artery may be increased in size if pulmonary hypertension is present. Spontaneous contrast (smoke) may be visible in the left atrium, left ventricle, and aorta. When present at rest, this echocardiographic abnormality is most often associated with low flow states and

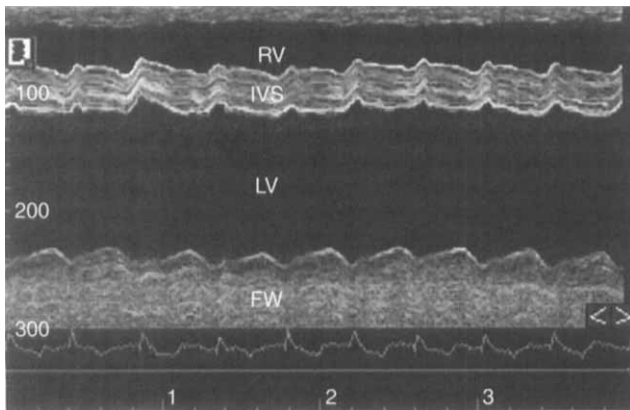


Figure 11.6-1 M-mode of the left ventricle obtained from the right parasternal window using a 2.5-MHz transducer. Note the minimal thickening of the interventricular septum and the left ventricular free wall during systole. RV, Right ventricle; IVS, interventricular septum; LV, left ventricle; FW, left ventricular free wall. (Courtesy Virginia Reef, University of Pennsylvania School of Veterinary Medicine, Philadelphia, Pa.)

poor cardiac output. Echocardiography performed after exercise may be helpful in detecting horses that have borderline resting myocardial function but develop left ventricular dysfunction immediately after exercise. Concurrent radiotelemetric assessment of the ECG during exercise can be helpful to reveal intermittent dysrhythmias in horses that appear normal at rest. Cardiac catheterization demonstrates elevated right atrial, right ventricular, pulmonary arterial, pulmonary capillary wedge pressure, and left ventricular end-diastolic pressures. Right ventricular cardiomyopathy also has been seen in horses, but is rare. With this disease, right atrial and ventricular enlargement are present, and secondary tricuspid regurgitation often is detected with Doppler echocardiography. Abnormal right ventricular free wall and interventricular septal motion also may be appreciated.

TREATMENT

Treatment of the underlying etiology, if any is recognized, and control of secondary complications such as congestive heart failure or dysrhythmias are the goals of therapy. Positive inotropic drugs such as digoxin may be helpful by increasing cardiac contractility. Digoxin also slows AV nodal conduction and is therefore valuable in controlling supraventricular tachycardias. The recommended dose of digoxin is 0.01 to 0.02 mg/kg by mouth divided into two doses per day. The dose should be decreased if evidence exists of dehydration or renal disease, and any prerenal azotemia must be addressed before beginning therapy. Clinical signs of digoxin toxicity include gastrointestinal disturbances such as anorexia, colic, and diarrhea. Occasionally secondary dysrhythmias occur. Therefore appetite, fecal consistency, cardiac rhythm, and electrolyte levels should be monitored during therapy. Therapeutic drug monitoring may be helpful to ensure that a therapeutic blood concentration is maintained. The trough blood level should be 1 to 2 ng/ml 6 to 8 hours after dos-

ing, and peak concentration 1 hour after dosing should not exceed 2.5 ng/ml.

Evaluation of the cardiac rhythm with continuous 24-hour Holter monitoring may be helpful in assessing the significance of intermittent dysrhythmias. Procainamide can be used at 25 to 35 mg/kg by mouth every 8 hours or 1 mg/kg/min IV up to a maximum of 20 mg/kg to control hemodynamically unstable ventricular dysrhythmias. Specific treatment of dysrhythmias is addressed in the chapter on arrhythmias and their treatment (see Chapter 11.4: "Cardiac Dysrhythmias").

Diuretics are essential in controlling congestive heart failure. The most commonly used diuretic in veterinary medicine is furosemide, a loop diuretic. The recommended dose for furosemide is 1 to 2 mg/kg orally, intramuscularly, or intravenously twice daily or as needed to control pulmonary edema. Afterload reducers are useful in the treatment of dilated cardiomyopathy in humans and small animals. Limited pharmacodynamic studies have been performed in the horse; however, angiotensin-converting enzyme inhibitors such as enalapril appear subjectively to be helpful at 0.5 mg/kg orally, once or twice per day. Alternatively, hydralazine can be used for afterload reduction and is less cost-prohibitive in the horse. The recommended dose of hydralazine is 0.5 to 1.5 mg/kg orally, twice daily. Corticosteroids may be helpful in animals with toxemia; however, their use should be avoided if severe congestive heart failure is present or evidence exists of an infectious etiology.

PROGNOSIS

The prognosis for a horse with dilated cardiomyopathy and congestive heart failure is grave. With monensin toxicity, echocardiography in general, and the shortening fraction in particular, are the best predictors of outcome. Horses with shortening fractions less than 20% have a grave prognosis for life, and prolonged stall rest with minimal stimulation is recommended. Dysrhythmias can develop months later in some monensin-exposed horses and probably are associated with previously undiagnosed myocardial scarring. Cardiac rhythm and myocardial function should be reevaluated every 4 to 6 months the first year after ionophore exposure. Horses with evidence of pulmonary hypertension, congestive heart failure, or dysrhythmias should not be ridden or driven because of risk of sudden death and human injury.

Supplemental Readings

- Guarda F, Giraldo A, Gagna C et al: Contribution to the study of fibro-adipous cardiomyopathy of the right ventricle in horses. *Ippologia* 1999; 10:45-54.
- Martin BB, Reef VB, Parente EJ et al: Causes of poor performance of horses during training, racing, or showing: 348 cases (1992-1996). *J Am Vet Med Assoc* 2000; 216:554-558.
- Reef VB, McGuirk SM: Diseases of the cardiovascular system. In Smith BP (ed): *Large Animal Internal Medicine*, ed 2, pp 507-549. Philadelphia, Mosby, 1996.
- Reef VB: Cardiovascular ultrasound. In Reef VB: *Equine Diagnostic Ultrasound*, pp 215-272. Philadelphia, WB Saunders, 1998.
- Reef VB: Stress echocardiography and its role in performance assessment. *Vet Clin North Am Equine Pract* 2001; 17:179-189.

CHAPTER 11.7

Acquired Pericardial Disease

MEG M. SLEEPER

Philadelphia, Pennsylvania

Pericarditis, or inflammation of the pericardium, is uncommon in horses and is often idiopathic. Current history of respiratory disease is common, and possible underlying causes include trauma, septicemia, pneumonia or pleuritis, equine influenza or viral arteritis, congestive heart failure, or (uncommonly) neoplasia. The increasing availability of more sophisticated diagnostics, such as viral immune titers, viral isolation, immunohistochemistry, and pericardial and myocardial biopsies, will ultimately reduce the number of idiopathic cases. Successful outcome is likely with early recognition and aggressive therapy.

Pericardial effusion results in decreased distensibility of the heart. This leads to increased ventricular end-diastolic pressure, which impairs diastolic filling. Venous return decreases as atrial pressure rises, and myocardial perfusion is reduced. Cardiac output and arterial pressure decrease. Initially, compensatory mechanisms of vasoconstriction, tachycardia, and sodium and water retention help preserve cardiac output, but eventually signs of heart failure develop. Pericarditis can be classified as primarily effusive or fibrinous. With the effusive form, the hemodynamic consequences are a result of the physical presence of the fluid. Constrictive pericarditis may follow the fibrinous form with reduction in ventricular compliance secondary to fibrinous or fibrotic involvement of the pericardium and epicardium. Consequently, removal of the fluid is of minimal value in fibrinous pericarditis, whereas it is essential in the effusive form.

CLINICAL SIGNS

Clinical signs can be variable depending on the underlying etiology of pericardial disease, the amount of effusion, and the rate of fluid accumulation. When the fluid accumulates gradually, pericardial stretching allows intrapericardial pressure to remain low in the face of gradually accumulating pericardial effusion until distention is severe. Clinical signs may be vague and include fever, weight loss, depression, anorexia, and exercise intolerance. Tachycardia is often present, particularly as cardiac output decreases. Heart sounds are muffled, and cardiac tamponade may be present. Cardiac tamponade occurs when intrapericardial pressure exceeds right ventricular filling pressure. If tamponade is present, clinical signs associated with right-sided congestive heart failure are common. These signs include jugular pulses and venous distention, ventral and subcutaneous edema, and ascites. Pericardial friction rubs may be audible, but the splashing sounds that are so typical in cows with trau-

matic reticulopericarditis are uncommon unless a penetrating wound is the underlying cause. Pericardial friction rubs are scratching, high-pitched sounds that classically have three components associated with atrial systole, ventricular systole, and rapid ventricular filling in early diastole.

Respiratory distress may be present, particularly if pericardial disease occurs in conjunction with pleuro-pneumonia or pleuritis. Dorsal displacement of the ventral lung border, caused by pleural effusion as well as enlargement of the pericardial sac, results in decreased breath sounds in the ventral thorax. This finding also occurs in horses with pleuropneumonia, however, unlike the situation in cases of pericarditis, the heart sounds are not usually muffled with these diseases. Peripheral pulses are often weak, and mucous membranes vary from pale to congested or cyanotic. The capillary refill time may be normal or prolonged.

LABORATORY FINDINGS

Clinical laboratory abnormalities are variable, nonspecific, and can include changes such as a stress leukogram, evidence of infection, hyperfibrinogenemia, hypoalbuminemia, prerenal azotemia, and hyponatremia. If cardiac tamponade is present, liver enzymes and indices of kidney function may be abnormal because of reduced cardiac output with decreased organ perfusion and/or hepatic passive congestion. Elevated peripheral and pericardial eosinophils occur with eosinophilic pericarditis. Titers for influenza, equine herpesvirus-1 (EHV-1), and equine arteritis virus should be evaluated. Cardiac isoenzymes may also be useful to determine if concurrent myocarditis is present. Central venous pressure will be elevated if cardiac tamponade is present.

The electrocardiogram (ECG) is often of diminished amplitude, however, this change is nonspecific and also can be seen in cases of pleural effusion, chronic obstructive pulmonary disease, or chronic pleuritis. Electrical alternans, beat-to-beat voltage variation of the QRS complex, is pathognomonic for pericardial effusion and occurs because of swinging of the heart within the pericardium with each beat. Slurring of the ST segment and/or dysrhythmias may occur but are not specific for pericardial disease. Radiography may be helpful, particularly in assessing a respiratory component, but echocardiography is much more useful to evaluate the degree of cardiac compromise. The cardiac silhouette can be enlarged or normal if the amount of pericardial effusion is small.

Echocardiography is the modality of choice for the di-

agnosis and treatment of pericardial disease, and allows characterization of the type of fluid present. Pericardial fluid can be seen as an anechoic to hypoechoic space that separates the parietal pericardium from the epicardial surface of the heart. Fibrin is hypoechoic to hyperechoic and variably distributed throughout the pericardium or on the surface of the heart. It usually has a shaggy appearance. With large-volume pericardial effusions, the heart may swing dramatically within the fluid and pericardial sac. Respiratory variations in ventricular filling are often detected in horses with pericardial effusions of large volume and cardiac tamponade. These variations are an increase in right ventricular size and decrease in left ventricular size on inspiration. If cardiac tamponade is present, cardiac chamber sizes will be smaller than normal with right atrial collapse during diastole. Right ventricular collapse may also be present, particularly as tamponade worsens. Similar to the changes in ventricular filling, Doppler-measured blood flows vary with respiration. In cases of constrictive pericarditis, abrupt cessation of ventricular filling in late diastole is apparent with two-dimensional real-time echocardiography and Doppler echocardiography. Pericardial thickening may or may not be appreciable. Echocardiography is also very helpful for guidance during pericardiocentesis and for monitoring fluid reaccumulation and fibrin resolution.

TREATMENT

Pericardiocentesis, with or without pericardial lavage, are treatments of choice when effusions are moderate to severe and compromising cardiac function. The optimal location for pericardiocentesis should be chosen with the aid of echocardiography, and is often the fifth intercostal space at the level of the costochondral junction. After surgical preparation and local infiltration of anesthesia, a stab incision should be performed to reduce tissue resistance and allow the location of the apparatus to be sensitively detected while it is passed through tissues. Placement of a large-bore, French Argyle (Tyco Healthcare Group, Mansfield, Mass.) chest tube (16 to 28 Fr) allows aggressive lavage. Alternatively, a 10-gauge catheter-over-needle system can be used. The ECG should be monitored throughout the procedure because dysrhythmias will often be stimulated if the needle contacts the myocardium. The lumen of the cannula should be closed with a stopcock to minimize risk of pneumothorax. When the apparatus contacts the pericardium, it will begin to move rhythmically with the movements of the pericardium. The tube or catheter is then advanced through the pericardium and a sample of fluid can be taken for cytology, viral isolation, and for aerobic and anaerobic culture and antimicrobial sensitivity. Bacterial culture of pericardial fluid is often unrewarding, but it is worthwhile if sepsis is likely. If respiratory disease is evident, culture and cytology of pleural fluid and/or transtracheal wash fluid may also be worthwhile. A concurrent echocardiogram is useful to verify placement of the catheter within the pericardium, and to evaluate the amount of residual fluid.

Catheters can be left in the pericardium until fluid production has decreased significantly. This decrease is indicated by a minimal amount of fluid visible with echocar-

diography, and drainage of less than 1 L of effusion per day. Between uses, the drain should be clamped or plugged with a sterile syringe. Twice-daily lavage of the pericardial sac with isotonic fluids that contain antimicrobials can be used to remove fibrin, bacteria, immune complexes, and inflammatory cells and their byproducts. Some authors recommend leaving 1 L of pH-adjusted polyionic fluid that contains antimicrobial drugs in the pericardial sac until the next drainage period. This technique appears particularly beneficial in cases of septic pericarditis when it may be advantageous to have high drug concentrations in the pericardial fluid. High local concentrations of antimicrobials may be necessary because of the rapid inactivation of many antimicrobials by fibrin. Sodium penicillin G and gentamicin have been used successfully in pericardial lavage fluids.

An alternative approach to indwelling pericardial drainage is intermittent pericardiocentesis performed as needed on the basis of echocardiographic findings. This approach has several theoretic benefits that include avoidance of an inflammatory response to an indwelling catheter, avoidance of instillation of pathologic organisms or an ascending infection, and less removal of beneficial, endogenous proteins such as tissue plasminogen factor. Intermittent pericardiocentesis requires frequent echocardiography to assess reaccumulation of pericardial effusion.

Pericardiectomy and pericardial stripping have been useful in humans and dogs. However, very few partial pericardiectomies have been performed in the horse. Fortunately, pericardial disease is rare in the horse, and the constrictive form is exceedingly uncommon.

Additional therapy should be given on the basis of the specific etiology. Culture results should direct antibiotic choice, but if cultures are not available, broad-spectrum, bactericidal antibiotics should be chosen. Antimicrobial therapy can be discontinued when septic pericarditis has resolved, or when cytology and bacterial culture show the disease is not bacterial in origin. Nonsteroidal antiinflammatory drugs may help to control signs of pain. Excessive pleural effusion should be removed. However, once cardiac tamponade is treated, the ensuing diuresis will result in resolution of mild-to-moderate pleural effusion and ascites. Furosemide is contraindicated because administration of this drug results in reduced preload that leads to a further compromise of cardiac output. Corticosteroids appear to be beneficial by decreasing the immune-mediated sequelae of viral infections, particularly in cases of fibrinous pericarditis, but should not be used if evidence exists of bacterial infection. Echocardiography is helpful to confirm removal of pericardial effusion. If not available, clinical responses such as decreased heart rate, reduced central venous pressure (indicated by decreased venous distention and jugular pulses), and improved pulse quality should be used to assess the animal's status. The ECG should also show an increase in complex amplitude after removal of pericardial effusion.

Supplemental Readings

Bernard W, Reef VB, Clark SE et al: Pericarditis in horses: six cases (1982-1986). *J Am Vet Med Assoc* 1990; 196:468-471.

- Dill S: Fibrinous pericarditis. In Robinson, NE (ed): *Current Therapy in Equine Medicine*, 2nd edition, pp 171-173, Philadelphia, WB Saunders, 1987.
- Hardy J, Robertson JT, Reed SM: Constrictive pericarditis in a mare: attempted treatment by partial pericardiectomy. *Equine Vet J* 1992; 24:151-154.
- Lorell BH: Pericardial diseases. In Braunwald E (ed): *Heart Disease*, 5th edition, pp 1478-1534, Philadelphia, WB Saunders, 1997.
- Reef VB: Cardiovascular ultrasound. In *Equine Diagnostic Ultrasound*, pp 215-272, Philadelphia, WB Saunders, 1998.
- Reef VB, Gentile DG, Freeman DE: Successful treatment of pericarditis in a horse. *J Am Vet Med Assoc* 1984; 185:94-97.
- Reef VB, McGuirk SM: Diseases of the cardiovascular system. In Smith BP (ed): *Large Animal Internal Medicine*, 2nd edition, pp 507-549, Philadelphia, Mosby, 1996.
- Sage AM, Worth L: Fever: endocarditis and pericarditis. In Marr C (ed): *Cardiology of the Horse*, pp 256-268, Philadelphia, WB Saunders, 1999.
- Voros K, Felkai C, Szilagyi Z et al: Two-dimensional echocardiographically guided pericardiocentesis in a horse with traumatic pericarditis. *J Am Vet Med Assoc* 1991; 198:1953-1956.
- Worth LT, Reef VB: Pericarditis in horses: 18 cases (1986-1995). *J Am Vet Med Assoc* 1998; 212: 248-253.

CHAPTER 11.8

Aortic Root Disease

ANNETTE LEROUX
Beechhurst, New York

The term *aortic root disease* refers to a group of disease entities that involve the proximal portion of the aorta and represent a continuum of pathologic processes that affect this specific portion of the vessel. Clinical signs associated with aortic root disease may be absent or may include sudden death depending on the severity of pathology involved. This disease classification includes aneurysms of the aortic root, aortocardiac fistulas, and complete rupture of the aortic root.

AORTIC ANEURYSMS

Aneurysms of the aortic root (sinus of Valsalva) have been detected as incidental findings on postmortem examination, in association with aortic regurgitation murmurs or other cardiac disease, or as incidental findings on echocardiographic examination. These aneurysms may be congenital or acquired, however, most documented reports of such aneurysms in the horse indicate that the majority of cases are acquired. Although etiologic factors have not been positively determined, these aneurysms are thought to have a similar etiology as aortocardiac fistulas and aortic rupture.

Clinical signs may be absent in affected horses, or one or more cardiac murmurs may be present on auscultation. A murmur of aortic insufficiency is more commonly documented in affected horses, and may be caused by intimal changes within the aortic root and valve support structure. Other murmurs may be evident as incidental findings or may be the result of physical disruption of normal blood flow by the aneurysm. If tearing of the aneurysm has occurred, cardiac arrhythmias may be present. These arrhythmias are commonly ventricular tachycardia or ventricular premature contractions. Signs of generalized distress may be apparent and may be misinterpreted as colic.

Diagnosis is confirmed by echocardiographic examination. Ultrasonographic findings include a focal dilation or ballooning of the aortic root, typically located in the right coronary sinus. Such an aneurysm can be distinguished from a ventricular septal defect based upon its more dorsal location and the pattern of blood flow on pulsed-wave or color-flow Doppler examination. An intact aneurysm may demonstrate turbulent flow within its lumen. If partial tearing of the aneurysm has occurred, turbulent blood flow is often demonstrated extending into the right ventricle, or less frequently, into the right atrium. In addition to pulsed-wave and color-flow Doppler, bubble contrast studies may be used to determine the presence of an aortocardiac fistula created by tearing of the aneurysm.

No treatment is currently available for horses with an aneurysm of the aortic sinus. Those animals so diagnosed should not be ridden or driven, because they are considered at high risk for rupture of the aneurysm. In one reported case, an aortic aneurysm resulted in impairment of closure of one of the tricuspid valve leaflets and ultimately resulted in severe tricuspid insufficiency and subsequent right-sided heart failure.

AORTOCARDIAC FISTULAS

As mentioned previously, an aortocardiac fistula may develop secondary to partial tearing of an aortic aneurysm. The disease process typically involves rupture of the right aortic sinus and creation of a communicating tract with the right ventricle, right atrium, or septal myocardium. Communication with the left ventricle is also possible, although far less common. Although this condition tends to affect older stallions, its incidence is not limited by sex or age. The etiology of the condition has not been conclusively determined, and possible factors include congenital deformity of the media of the aorta and annulus fi-

- Dill S: Fibrinous pericarditis. In Robinson, NE (ed): *Current Therapy in Equine Medicine*, 2nd edition, pp 171-173, Philadelphia, WB Saunders, 1987.
- Hardy J, Robertson JT, Reed SM: Constrictive pericarditis in a mare: attempted treatment by partial pericardiectomy. *Equine Vet J* 1992; 24:151-154.
- Lorell BH: Pericardial diseases. In Braunwald E (ed): *Heart Disease*, 5th edition, pp 1478-1534, Philadelphia, WB Saunders, 1997.
- Reef VB: Cardiovascular ultrasound. In *Equine Diagnostic Ultrasound*, pp 215-272, Philadelphia, WB Saunders, 1998.
- Reef VB, Gentile DG, Freeman DE: Successful treatment of pericarditis in a horse. *J Am Vet Med Assoc* 1984; 185:94-97.
- Reef VB, McGuirk SM: Diseases of the cardiovascular system. In Smith BP (ed): *Large Animal Internal Medicine*, 2nd edition, pp 507-549, Philadelphia, Mosby, 1996.
- Sage AM, Worth L: Fever: endocarditis and pericarditis. In Marr C (ed): *Cardiology of the Horse*, pp 256-268, Philadelphia, WB Saunders, 1999.
- Voros K, Felkai C, Szilagyi Z et al: Two-dimensional echocardiographically guided pericardiocentesis in a horse with traumatic pericarditis. *J Am Vet Med Assoc* 1991; 198:1953-1956.
- Worth LT, Reef VB: Pericarditis in horses: 18 cases (1986-1995). *J Am Vet Med Assoc* 1998; 212: 248-253.

CHAPTER 11.8

Aortic Root Disease

ANNETTE LEROUX
Beechhurst, New York

The term *aortic root disease* refers to a group of disease entities that involve the proximal portion of the aorta and represent a continuum of pathologic processes that affect this specific portion of the vessel. Clinical signs associated with aortic root disease may be absent or may include sudden death depending on the severity of pathology involved. This disease classification includes aneurysms of the aortic root, aortocardiac fistulas, and complete rupture of the aortic root.

AORTIC ANEURYSMS

Aneurysms of the aortic root (sinus of Valsalva) have been detected as incidental findings on postmortem examination, in association with aortic regurgitation murmurs or other cardiac disease, or as incidental findings on echocardiographic examination. These aneurysms may be congenital or acquired, however, most documented reports of such aneurysms in the horse indicate that the majority of cases are acquired. Although etiologic factors have not been positively determined, these aneurysms are thought to have a similar etiology as aortocardiac fistulas and aortic rupture.

Clinical signs may be absent in affected horses, or one or more cardiac murmurs may be present on auscultation. A murmur of aortic insufficiency is more commonly documented in affected horses, and may be caused by intimal changes within the aortic root and valve support structure. Other murmurs may be evident as incidental findings or may be the result of physical disruption of normal blood flow by the aneurysm. If tearing of the aneurysm has occurred, cardiac arrhythmias may be present. These arrhythmias are commonly ventricular tachycardia or ventricular premature contractions. Signs of generalized distress may be apparent and may be misinterpreted as colic.

Diagnosis is confirmed by echocardiographic examination. Ultrasonographic findings include a focal dilation or ballooning of the aortic root, typically located in the right coronary sinus. Such an aneurysm can be distinguished from a ventricular septal defect based upon its more dorsal location and the pattern of blood flow on pulsed-wave or color-flow Doppler examination. An intact aneurysm may demonstrate turbulent flow within its lumen. If partial tearing of the aneurysm has occurred, turbulent blood flow is often demonstrated extending into the right ventricle, or less frequently, into the right atrium. In addition to pulsed-wave and color-flow Doppler, bubble contrast studies may be used to determine the presence of an aortocardiac fistula created by tearing of the aneurysm.

No treatment is currently available for horses with an aneurysm of the aortic sinus. Those animals so diagnosed should not be ridden or driven, because they are considered at high risk for rupture of the aneurysm. In one reported case, an aortic aneurysm resulted in impairment of closure of one of the tricuspid valve leaflets and ultimately resulted in severe tricuspid insufficiency and subsequent right-sided heart failure.

AORTOCARDIAC FISTULAS

As mentioned previously, an aortocardiac fistula may develop secondary to partial tearing of an aortic aneurysm. The disease process typically involves rupture of the right aortic sinus and creation of a communicating tract with the right ventricle, right atrium, or septal myocardium. Communication with the left ventricle is also possible, although far less common. Although this condition tends to affect older stallions, its incidence is not limited by sex or age. The etiology of the condition has not been conclusively determined, and possible factors include congenital deformity of the media of the aorta and annulus fi-

brosis, or acquired degeneration and weakening of the aortic wall from preexisting cardiac disease.

Clinical signs at the onset of fistula formation are often mistaken for abdominal pain. Sweating, pawing, recumbency, or collapse may be present, and evaluation of the cardiovascular system may reveal tachycardia, bounding arterial pulses, and a characteristic continuous murmur present in the right fourth intercostal space. Additional murmurs may be present as incidental findings or related to the disease process.

Diagnosis is confirmed by ultrasonographic examination. Two-dimensional echocardiographic examination is typically sufficient to document the fistula, although Doppler color flow and/or contrast agents may be used to further quantify blood flow and turbulence associated with the defect. Evidence of direct communication of the aortic sinus with the right ventricle or atrium, septal myocardium, or left ventricle may be visible. If dissection within the septal myocardium has occurred, it usually appears as an anechoic tract within the proximal portion of the septum. Accompanying findings may include ventricular or atrial enlargement and/or vibration of the septal leaflet of the tricuspid valve from turbulent flow through the fistula. Electrocardiographic examination may reveal arrhythmias, most commonly that of monoform ventricular tachycardia. Atrial fibrillation has also been associated with these fistulas.

Treatment is largely palliative and directed at stabilizing the cardiovascular system and addressing life-threat-

ening arrhythmias. Lidocaine, quinidine gluconate, and magnesium sulfate have been used in the treatment of monoform ventricular tachycardia with variable results. The reader is referred to the section on cardiac arrhythmias for further descriptions and drug dosages (see Chapter 11.4: "Cardiac Dysrhythmias").

The prognosis for these horses must be considered guarded. Although there have been reported cases that survived at least 4 years after diagnosis, the majority of affected animals die or are euthanized within days or a few months after diagnosis.

Unlike an aortocardiac fistula, in which partial tearing of the vessel has occurred, complete rupture of the aortic root is often sudden, without warning, and results in no clinical signs other than sudden death. Although rupture can occur at any time, it is often associated with exercise or strenuous activity, as in the case of stallions during breeding. Diagnosis is confirmed by postmortem examination. (See Chapter 11.9: "Vascular Diseases" for a more detailed description of aortic root ruptures.)

Supplemental Readings

Marr CM, Reef VB, Brazil TJ et al: Aorto-cardiac fistulas in seven horses. *Vet Radiol Ultrasound* 1998; 39:22-31.

Sleeper MM, Durando MM, Miller M et al: Aortic root disease in four horses. *J Am Vet Med Assoc* 2001; 219:491-496.

CHAPTER 11.9

Vascular Diseases

ANNETTE LEROUX
Beechhurst, New York

JUGULAR VEIN THROMBOPHLEBITIS/ THROMBOSIS

Thrombophlebitis is inflammation of the wall of a peripheral vein with partial or complete luminal occlusion by a thrombus. This condition is one of the more common peripheral vascular disorders that occur in the horse. Although any peripheral vein may be susceptible, the jugular vein is most often affected. Complications from venipuncture or catheterization are often etiologic factors, although trauma and a hypercoagulable state that results from septicemia or other systemic illness may predispose to this condition.

Clinical Signs

Clinical signs associated with acute thrombophlebitis include heat, swelling, and palpable sensitivity of the affected vein and adjacent area. If occlusion of the jugular vein is severe, distention of the smaller facial vessels on the af-

ected side may be prominent. Occlusion of both jugular veins may also result in facial edema and impaired exercise ability. Thrombosis of the vein may occur in concert with the acute phase of inflammation or as a sequel to the disease process. The thrombosed vein will often feel firm or "corded" on palpation. Digital occlusion of the jugular vein near the thoracic inlet will often result in delayed proximal filling of the vessel. This delay in filling is again dependent on the inflammatory response and size of the thrombus.

Diagnosis

Diagnosis is made on the basis of clinical history and palpation of the affected vessel and surrounding area. Heat and sensitivity may be absent if the condition is more chronic, and peripheral distention of proximal superficial

brosis, or acquired degeneration and weakening of the aortic wall from preexisting cardiac disease.

Clinical signs at the onset of fistula formation are often mistaken for abdominal pain. Sweating, pawing, recumbency, or collapse may be present, and evaluation of the cardiovascular system may reveal tachycardia, bounding arterial pulses, and a characteristic continuous murmur present in the right fourth intercostal space. Additional murmurs may be present as incidental findings or related to the disease process.

Diagnosis is confirmed by ultrasonographic examination. Two-dimensional echocardiographic examination is typically sufficient to document the fistula, although Doppler color flow and/or contrast agents may be used to further quantify blood flow and turbulence associated with the defect. Evidence of direct communication of the aortic sinus with the right ventricle or atrium, septal myocardium, or left ventricle may be visible. If dissection within the septal myocardium has occurred, it usually appears as an anechoic tract within the proximal portion of the septum. Accompanying findings may include ventricular or atrial enlargement and/or vibration of the septal leaflet of the tricuspid valve from turbulent flow through the fistula. Electrocardiographic examination may reveal arrhythmias, most commonly that of monoform ventricular tachycardia. Atrial fibrillation has also been associated with these fistulas.

Treatment is largely palliative and directed at stabilizing the cardiovascular system and addressing life-threat-

ening arrhythmias. Lidocaine, quinidine gluconate, and magnesium sulfate have been used in the treatment of monoform ventricular tachycardia with variable results. The reader is referred to the section on cardiac arrhythmias for further descriptions and drug dosages (see Chapter 11.4: "Cardiac Dysrhythmias").

The prognosis for these horses must be considered guarded. Although there have been reported cases that survived at least 4 years after diagnosis, the majority of affected animals die or are euthanized within days or a few months after diagnosis.

Unlike an aortocardiac fistula, in which partial tearing of the vessel has occurred, complete rupture of the aortic root is often sudden, without warning, and results in no clinical signs other than sudden death. Although rupture can occur at any time, it is often associated with exercise or strenuous activity, as in the case of stallions during breeding. Diagnosis is confirmed by postmortem examination. (See Chapter 11.9: "Vascular Diseases" for a more detailed description of aortic root ruptures.)

Supplemental Readings

Marr CM, Reef VB, Brazil TJ et al: Aorto-cardiac fistulas in seven horses. *Vet Radiol Ultrasound* 1998; 39:22-31.

Sleeper MM, Durando MM, Miller M et al: Aortic root disease in four horses. *J Am Vet Med Assoc* 2001; 219:491-496.

CHAPTER 11.9

Vascular Diseases

ANNETTE LEROUX
Beechhurst, New York

JUGULAR VEIN THROMBOPHLEBITIS/ THROMBOSIS

Thrombophlebitis is inflammation of the wall of a peripheral vein with partial or complete luminal occlusion by a thrombus. This condition is one of the more common peripheral vascular disorders that occur in the horse. Although any peripheral vein may be susceptible, the jugular vein is most often affected. Complications from venipuncture or catheterization are often etiologic factors, although trauma and a hypercoagulable state that results from septicemia or other systemic illness may predispose to this condition.

Clinical Signs

Clinical signs associated with acute thrombophlebitis include heat, swelling, and palpable sensitivity of the affected vein and adjacent area. If occlusion of the jugular vein is severe, distention of the smaller facial vessels on the af-

ected side may be prominent. Occlusion of both jugular veins may also result in facial edema and impaired exercise ability. Thrombosis of the vein may occur in concert with the acute phase of inflammation or as a sequel to the disease process. The thrombosed vein will often feel firm or "corded" on palpation. Digital occlusion of the jugular vein near the thoracic inlet will often result in delayed proximal filling of the vessel. This delay in filling is again dependent on the inflammatory response and size of the thrombus.

Diagnosis

Diagnosis is made on the basis of clinical history and palpation of the affected vessel and surrounding area. Heat and sensitivity may be absent if the condition is more chronic, and peripheral distention of proximal superficial

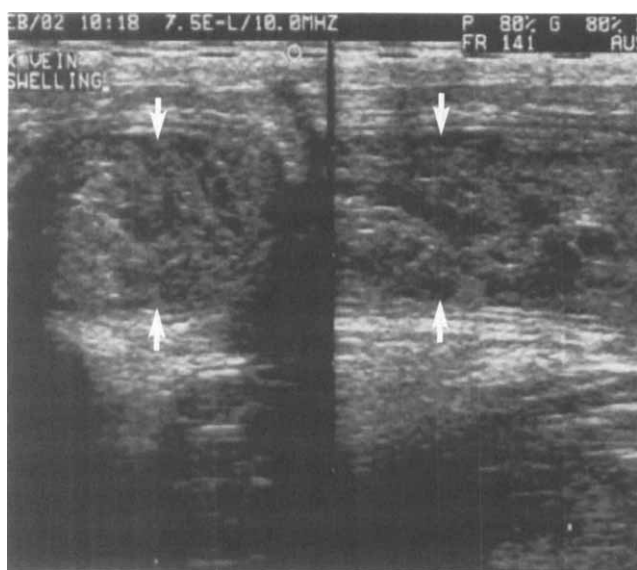


Figure 11.9-1 Transverse (left) and longitudinal (right) ultrasonographic images of a thrombus within the maxillary vein. Note the heterogeneous, echogenic appearance of the thrombus, which is occluding the lumen of the vein. Images were obtained with a 7.5-MHz linear transducer. Arrows mark boundaries of vein.

vessels may be diminished if collateral circulation has had sufficient time to develop. Ultrasonographic evaluation can confirm the diagnosis by demonstrating thickening of the vessel wall and compromise of the vessel lumen. If a thrombus is present within the vessel lumen, its appearance may be variable; it may appear homogeneously hyperechoic or heterogeneously anechoic, hypoechoic, or hyperechoic (Figure 11.9-1). A surrounding fibrin network may also be present.

Anaerobic infection should be suspected if multiple hyperechoic foci (gas echoes) are present within the thrombus, particularly if the patient has fever, leukocytosis, neutrophilia, and hyperfibrinogenemia. Pulsed-wave or color-flow Doppler ultrasonography or saline contrast venography may be used to evaluate the reduction in blood flow within the vessel. If septic thrombophlebitis is suspected, culture of the involved catheter and/or a needle aspirate of a pocket within the thrombus are recommended. Both aerobic and anaerobic culture of the sample are indicated and antibiotic sensitivity of bacteria should be determined. Commonly cultured gram-positive organisms include β -hemolytic *Streptococcus* spp., non-group-D α -hemolytic *Streptococcus* species, and *Staphylococcus aureus*. Gram-negative organisms commonly cultured include *Pasteurella/Actinobacillus* spp., *Escherichia coli*, and *Klebsiella pneumoniae*.

In cases of acute thrombophlebitis, the presence of any cardiac murmur should be ascertained by auscultation, because septic thrombi may migrate to the heart and induce a bacterial endocarditis. If a previously undetected murmur is present, echocardiographic evaluation of the valve leaflets should be performed. Although rare, pulmonary thromboembolism may result from severe cases of jugular thrombophlebitis.

Treatment

Treatment is directed at reducing the inflammatory response within the affected vessel and combating infection. Suspected septic thrombophlebitis should be treated with broad-spectrum antibiotics until culture and sensitivity results are obtained. Penicillin (procaine penicillin G, 22,000 IU/kg IM q12h or potassium penicillin, 22,000 IU/kg IV q6h) combined with an aminoglycoside (gentamicin sulfate, 6.6 mg/kg IV or IM q24h) is an appropriate therapeutic regimen while culture results are pending. If anaerobic infection is suspected from clinical signs and findings from the ultrasonographic examination, addition of metronidazole (15 mg/kg PO q6h-q8h) to the treatment protocol is recommended. Use of the affected vessel for injections should be avoided. Hot packing and topical administration of dimethyl sulfoxide may alleviate swelling of the area. Systemic therapy with nonsteroidal antiinflammatory drugs such as flunixin meglumine or phenylbutazone is also recommended.

Occlusion of both jugular veins may necessitate a temporary reduction in training if facial edema becomes a problem. Recanalization of the affected vessel/vessels, combined with the development of collateral circulation, will in time allow for the resolution of facial edema and return to exercise. For those patients that have responded poorly to medical management, surgical resection or reconstruction of the occluded vein may be attempted. Successful reconstruction of the jugular vein has been reported using a saphenous vein graft. Thrombolytic and anticoagulant treatment in the horse has thus far met with limited success.

THROMBOEMBOLISM

Although any arterial vessel is susceptible to thromboembolism, aortoiliac thrombosis is one of the more commonly documented examples of this disease process in the horse. A thrombus may form or lodge within the terminal aorta and/or one or all of its branches, the internal or external iliac arteries. The cranial mesenteric artery is another vessel historically affected by thromboembolism. Although uncommon, pulmonary thromboembolism has been documented in the horse, and may occur as a sequel to severe jugular vein thrombophlebitis. Thrombosis of limb arteries has also been described.

Proposed etiologic factors for thromboembolism include parasite migration (*Strongylus vulgaris* in the case of the cranial mesenteric artery), systemic infections (septicemia), endotoxemia, vasculitis, and bacterial endocarditis. Endocarditis lesions that affect the right side of the heart typically lead to pulmonary emboli, whereas vegetative lesions that affect the left side of the heart typically result in embolization of the kidneys. Formation of thrombi is hypothesized to be the result of three pathologic mechanisms—induction of a hypercoagulable state, damage to the vascular endothelium, and development of turbulent blood flow within the affected vessel lumen.

When the cranial mesenteric artery is affected, the disease process is often referred to as *thromboembolic colic*. This terminology is somewhat of a misnomer, however, because many horses affected by the condition do not have demonstrable emboli obstructing the intestinal

blood supply on postmortem examination. The disease process is associated with damage to the vascular endothelium of the aorta and cranial mesenteric artery by the migrating L4 larvae of *S. vulgaris*. It has been theorized that the endothelial damage caused by the parasite results in platelet aggregation and subsequent proximal thrombus formation. Release of vasoactive mediators (e.g., thromboxane) from the thrombus induces constriction of the arterial blood supply distal to the thrombus, which results in intestinal ischemia. In addition, the thrombus may mechanically reduce blood flow to the intestine, which is normally supplied by the cranial mesenteric artery and its branches. Severe enterocolitis may also result in thrombosis of vessels supplying the small and large intestine. This condition is proposed to be secondary to endotoxemia, antithrombin III deficiency, and activation of procoagulants.

Clinical Signs

Clinical signs of thromboembolism may be nonspecific and variable depending on which organ is affected. Horses with aortoiliac thrombosis can demonstrate ataxia, collapse, generalized discomfort, or exercise-related unilateral or bilateral hindlimb lameness. Delayed filling of the saphenous vein and a weak dorsal metatarsal artery pulse may be apparent if occlusion of the terminal vessels is severe. The temperature of the affected limb may be normal or cool, again depending on the degree of vascular compromise. Severely compromised limbs may be edematous and painful on palpation. Reproductive failure has been documented in breeding stallions. The general demeanor of the horse may be altered, and pain-related tachypnea and sweating might be evident during even mild exercise.

Clinical signs associated with thromboembolism of the abdominal aorta and cranial mesenteric artery include those referable to abdominal pain. Sweating, pawing, frequent lying down or pacing, tachycardia, diminished gastrointestinal sounds, injected mucous membranes, and lack of response to analgesic therapy all are supportive of the diagnosis, although obviously not confirmatory. Although the majority of horses today are maintained on an adequate intestinal parasite control program, history of poor deworming practices or a heavily infested environment should raise suspicions to the possibility of cranial mesenteric artery compromise. Horses with severe enterocolitis may be at increased risk for developing thrombosis of mesenteric vessels.

Clinical signs of pulmonary embolism include tachypnea, exercise intolerance, acute severe dyspnea, and physical examination findings consistent with pneumonia. Epistaxis may be evident if the embolism has resulted in pulmonary infarction. Because pulmonary embolism in horses is rare, clinical signs related to this condition may be inadvertently attributed to other disease processes that affect the respiratory or cardiac systems.

Diagnosis

Diagnosis of aortoiliac thromboembolism can usually be made on rectal examination. Findings may include a decrease in pulse quality of the terminal aorta and its branches, with

a firm intraluminal mass within one or more of the vessels. Rectal ultrasound is useful to confirm the diagnosis. Linear 5.0- or 7.5-MHz probes may be used to observe the affected vessels. Additionally, transverse views of the terminal aorta and four iliac arteries may be observed simultaneously with a 6.0-MHz microconvex probe. Sonographic findings may include an echogenic thrombus partially or completely occluding the terminal aorta and/or iliac arteries, sludging of blood proximal to the thrombus, and/or distention of the aorta proximal to the thrombus. Additional diagnostic modalities include digital subtraction angiography and first pass radionuclide angiography. Unlike digital subtraction angiography, the latter has the advantage of not requiring general anesthesia for the procedure.

Diagnosis of thromboembolic colic can be supported by clinical history, physical examination findings, and laboratory results, but ultimately it is made by exploratory laparotomy or postmortem exam. Distention of small intestinal loops on rectal examination, serosanguineous fluid and the presence of bacteria on abdominocentesis, and nasogastric reflux and pain refractory to analgesics indicate a surgical colic. Absence of a nonstrangulating intestinal lesion at surgery combined with devitalization of intestine supplied by the cranial mesenteric artery supports the diagnosis.

Diagnosis of pulmonary thromboembolism can be difficult. Clinical examination, progression of disease, and radiographic and ultrasonographic findings may be supportive. Ultrasonographic examination may demonstrate the thrombus if the most proximal portion of the artery is affected. Angiography and ventilation-perfusion pulmonary scintigraphy have been successfully used in small animals to diagnose the disease. As mentioned above, first pass radionuclide angiography has successfully diagnosed aortoiliac thromboembolism in the horse, and as such may be useful in the diagnosis of pulmonary thromboembolism.

Treatment

Treatment of aortoiliac thrombosis has met with limited success, and prognosis for future athletic performance must be guarded. Stall rest, antiinflammatory therapy, prolonged larvicidal deworming protocols, intravenous (IV) sodium gluconate therapy, and low molecular-weight dextran have all met with poor success, particularly in more chronic cases. Streptokinase, urokinase, and recombinant tissue plasminogen activators have been used in humans and small animals for treatment of thromboemboli, although their use and success rate in horses has been both limited and disappointing thus far. Recombinant tissue plasminogen activator, the newest of the thrombolytic therapies, is a fibrin-specific thrombolytic agent that catalyzes the conversion of plasminogen to plasmin, and whose activity is greatly enhanced when fibrin is present.

Treatment options for cranial mesenteric thromboembolism are limited given the nature of the disease process and the usual extent of compromised bowel. Peritonitis is often a secondary consequence of intestinal ischemia. Palliative measures include IV fluid therapy, broad-spectrum antibiotics, and nonsteroidal therapy for its analgesic, antiinflammatory, and antiendotoxic properties. Heparin has been used for its anticoagulant and

antiendotoxin properties. Despite therapy, the prognosis for this condition must be considered guarded.

The prognosis for pulmonary thromboembolism also must be guarded, and treatment is generally supportive in nature. If associated with an infectious process or a septic pneumonia, treatment is directed at the underlying cause.

ARTERIOVENOUS FISTULA

An arteriovenous fistula is defined as a direct communication between the arterial and venous circulations that excludes the capillary network. Such a fistula may be congenital or acquired. Congenital fistulas result from abnormal development of embryonic vascular tissue, whereas acquired fistulas often result from trauma such as wounds, injection complications, mass ligation of arteries and veins, or rupture of an aneurysm. Arteriovenous fistulas have also been associated with large vascular tumors such as hemangiomas and hemangiosarcomas. If large enough, they can induce hemodynamic abnormalities such as an elevated resting heart rate because of the increased effort needed to maintain normal cardiac output.

Clinical Signs

Clinical signs are varied and depend somewhat on the location of the arteriovenous fistula. Abnormal, distended, superficial vessels arranged in a tortuous pattern may be visible in any location, and an increase in temperature of the involved region may be present. A continuous bruit is sometimes auscultated in the affected area, and palpation may reveal a slight pulsation or fremitus. The partial pressure of oxygen (PO_2) distal to the fistula will be higher than the systemic venous PO_2 , and may be equal to that proximal to the fistula. With a large arteriovenous shunt of a distal extremity, skin ulceration of the affected limb can develop as a consequence of peripheral ischemia. Fistulas secondary to trauma usually are not painful, but they are often ulcerated and may hemorrhage. Arteriovenous fistulas located in limbs may result in peripheral edema and lameness. Large fistulas may result in a vagally mediated reduction in heart rate (Branham's sign) when manually compressed. This reduction occurs because compression leads to an elevation of arterial blood pressure from increased peripheral vascular resistance and blood volume.

Diagnosis

Diagnosis is based on clinical findings, but it may be confirmed by selective contrast angiography or Doppler (color flow, continuous wave, or pulsed-wave spectral) ultrasonography. Color-flow Doppler examination may reveal turbulent flow within the affected area, whereas spectral examination may reveal high-flow velocities, spectral broadening and signals above and below zero baselines. A continuous flow pattern that demonstrates arterial characteristics can be documented within the involved artery, through the fistula, and into the venous circulation. A complete cardiovascular exam should be performed in all affected individuals, because large arteriovenous fistulas can ultimately lead to heart failure as the result of prolonged elevation of cardiac workload.

Treatment

In humans, treatment of arteriovenous fistulas involves division and reconstruction of the affected vessels. Because this is often not feasible in the horse, surgical excision of the fistula is recommended for cosmetic reasons and for prevention of further injury and associated hemorrhage.

ARTERIAL RUPTURE

Arterial rupture is a well-documented event in the horse, and the more frequently documented cases involve the aorta, pulmonary, or uterine arteries. Although aortic root rupture has been documented most commonly in older breeding stallions, this condition has also been reported in older mares. Pulmonary artery rupture is typically seen in patients suffering from either heart failure and accompanying pulmonary artery distention, or chronic pulmonary hypertension from severe (longstanding) mitral insufficiency. This condition also has been documented in association with patent ductus arteriosus. Mares at or following parturition may rupture the uterine artery, or less commonly the middle uterine or utero-ovarian arteries. Other instances of arterial rupture include the internal carotid artery and smaller pulmonary vessels.

Etiologic factors associated with arterial rupture include congenital defects of the vessel wall, and in the case of breeding stallions, chronic intimal stress associated with hypertension during breeding. In mares, spontaneous rupture of the uterine or middle uterine artery, utero-ovarian, and/or external iliac arteries has been documented during and following parturition, and is thought to be caused by preexisting degenerative changes of the vessel wall in combination with the stresses associated with parturition (see Chapter 5.34: "Management of Postpartum Hemorrhages"). Rupture of the internal carotid artery is often the result of damage from a chronic mycotic or bacterial infection within the guttural pouch. Physiologic stresses experienced during intense exercise may rupture smaller pulmonary capillaries/arterioles in the syndrome of exercise-induced pulmonary hemorrhage (see Chapter 8.7: "Exercise-Induced Pulmonary Hemorrhage").

Clinical Signs

The clinical sign of spontaneous rupture of any large vessel such as the aorta or pulmonary artery is typically sudden death. Partial tearing or rupture of the aorta or pulmonary artery may produce signs that reflect acute cardiac decompensation, including collapse, elevated heart rate, pale mucous membranes, weak peripheral pulses, and overall distress which may manifest itself as colic, tremors, and/or extreme exercise intolerance. Sinus tachycardia is usually present, although junctional or ventricular tachycardias may occur. Clinical signs of tearing or rupture of the middle uterine artery or abdominal vessels reflect generalized hemorrhagic shock. Affected animals may demonstrate tachycardia, tachypnea with pale mucous membranes, poor capillary refill time, and weak peripheral pulse quality. Before rupture there may be no clinical signs in these horses. Signs of preexisting cardiac disease may be evident in some horses before rupture of the aorta

or pulmonary artery. Aortic regurgitation may be present before aortic root rupture. Mitral valve regurgitation combined with left atrial/ventricular enlargement and pulmonary artery enlargement often is present before rupture of the pulmonary artery.

Aortic root mineralization is sometimes documented on two-dimensional echocardiography, although this finding is not a reliable predictor of impending arterial rupture. As previously stated, pulmonary artery rupture is a sequel to left heart failure associated with severe chronic mitral regurgitation or chronic pulmonary hypertension. Echocardiography can be used to confirm heart failure with dilation of the main pulmonary artery or left and right pulmonary arteries.

Diagnosis

Diagnosis of acute rupture of the aorta or pulmonary artery is confirmed at necropsy. The typical location for aortic root rupture is the right sinus of Valsalva. Partial aortic rupture may be confirmed with echocardiography and either pulsed-wave or color-flow Doppler examination. Horses with partial aortic root rupture may demonstrate evidence of hemorrhage near the membranous portion of the interventricular septum, or apical infiltration into the muscle of the interventricular septum. Affected horses often have a low-pitched continuous murmur heard loudest over the right thorax. Monomorphic ventricular tachycardia often results from disruption of conduction tissue by the dissecting hematoma. In those horses that survive long enough for echocardiographic examination, partial tearing of the pulmonary artery may reveal flailing of the pulmonary valve and dissection of blood into adjacent tissues. Dilation of the artery will be evident, and the two-dimensional diameter of the artery will be greater than the two-dimensional diameter of the aorta. In mares with middle uterine artery rupture, rectal examination may reveal palpable swelling within the broad ligament.

Treatment

If treatment of patients suffering from partial rupture of the aorta or pulmonary artery is attempted, it is directed at generalized cardiac support and treatment of life threatening cardiac arrhythmias. If these horses survive the acute phase, treatment for congestive heart failure is prudent and includes inotropic support and diuretic and venodilator treatment. The reader is referred to the section on cardiac arrhythmias for discussion of drug choices and dosages (see Chapter 11.4: "Cardiac Dysrhythmias"). Affected horses have a grave prognosis, and should not be subjected to exercise or other strenuous activity that might endanger the lives of their handlers. If the decision is made for stallions of high breeding value to continue servicing mares, it must be made with the full knowledge of the risk of collapse and sudden death from further arterial rupture as a result of stress. Horses that have partial aortic root rupture with dissection of the endocardium may experience rupture into the right or left ventricle. Documented cases of partial aortic root rupture have reported survival times of as long as 12 months.

Treatment of mares with rupture of any of the major arteries within the reproductive tract should be directed at systemic stabilization and treatment of hemorrhagic shock. If arterial rupture occurs during parturition, the foal should be delivered as rapidly as possible. IV fluids are initially indicated, although subsequent IV fluid therapy or blood transfusions must be given carefully, because elevation of blood pressure may induce further hemorrhage. Prothrombotic agents such as aminocaproic acid and conjugated estrogens may be given to try to control hemorrhage and promote clotting. The mare should be kept as calm as possible, with strict stall rest for several weeks. Transport of the mare within the first several weeks of foaling is not recommended. Rectal examinations should not be performed unless further hemorrhage is suspected and/or the mare's clinical condition continues to deteriorate. Some individuals have advocated temporary weaning of the foal, as uterine contractions stimulated by oxytocin release during nursing may promote further hemorrhage.

Prevention of arterial rupture can be difficult, particularly if the horse lacks clinical signs that indicate the condition. Yearly prebreeding echocardiographic examinations of older breeding stallions may be prudent, particularly in those individuals with documented aortic or mitral insufficiency murmurs. Horses with evidence of severe mitral insufficiency and pulmonary artery enlargement should no longer be ridden or driven, as the risk of arterial rupture is significantly increased in these animals. Mares that have survived rupture of a major reproductive tract artery ideally should not be rebred because of the risk involved with future pregnancies and parturition.

PERIPHERAL ANEURYSM

A peripheral arterial aneurysm is a localized dilatation of a vessel wall caused by weakening of the wall structure. Aneurysms are infrequently diagnosed in horses, but of those reported cases aortic root aneurysm is the most common. Aortic root aneurysms are discussed in greater detail in the chapter on aortic root disease (see Chapter 11.8).

Trauma is often implicated in the development of aneurysms located in vessels of the extremities. Clinical signs include a soft fluctuant mass that is often not painful on palpation but has a strong pulsation. Diagnosis is made on the basis of clinical findings but can be confirmed with contrast angiography and ultrasonography. Treatment involves surgical excision in order to reduce the risk of trauma and subsequent hemorrhage, as well as to improve cosmetic appearance. Before surgical excision, contrast angiography can be used to determine the degree of collateral circulation of the affected vessel and to ascertain whether the vessel can be removed without risk of ischemic complications.

VASCULITIS/ARTERITIS

Vasculitis, an inflammatory process within the walls of blood vessels, may be a primary disease process but more often is a secondary sequela to a primary disease. Although all vessels are susceptible to the inflammatory process, postcapillary venules are typically affected in the horse. Equine viral arteritis is an exception because it

affects arterioles rather than venules. Etiologic factors associated with vasculitis/arteritis include infection, drug treatment, toxin exposure, parasitism, or (less frequently) neoplasia. The more commonly incriminated infectious processes associated with vasculitis include purpura hemorrhagica secondary to *Streptococcus equi* infections, equine infectious anemia, equine viral arteritis, and equine ehrlichiosis. Arteritis that results from parasite damage (verminous arteritis) has been described previously and often involves damage to the cranial mesenteric artery subsequent to migrating L4 *S. vulgaris* larvae. Idiopathic vasculitis has also been documented.

Pathologic changes associated with vasculitis are primarily those of a hypersensitivity response. Damage to vessel walls occurs from deposition of circulating immune complexes and leads to subsequent clinical signs associated with increased permeability of the vessel walls.

Clinical Signs

Clinical signs of vasculitis vary and depend on the disease process involved as well as the location of the damaged vessels. Cutaneous/subcutaneous edema is a common sign, and may be accompanied by erythema and crusting. Distal extremities and the ventrum are commonly affected. In more advanced cases, necrosis and ulceration of the extremities may occur. Purpura hemorrhagica patients may also have extensive edema of the face and neck. Mucous membranes may demonstrate petechiae or ecchymosis. Observable systemic signs may include depression, fever, anorexia, weight loss and/or lameness.

Diagnosis is often made on the basis of clinical signs and history, as well as response to therapy. Confirmation of actual vasculitis may be attempted with biopsy of cutaneous lesions. If the suspected etiology is infectious, appropriate diagnostic measures are recommended related to the suspected infectious agent.

Treatment

Treatment of vasculitis is largely symptomatic and supportive and, again, depends on the suspected etiology.

General care involves relief of edema. As such, hydrotherapy, pressure bandages, and antiinflammatory drugs are indicated to alleviate swelling of distal extremities and to relieve associated pain or discomfort. Mild exercise and diuretic therapy may also be of benefit in minimizing edema. In cases of suspected purpura hemorrhagica, administration of penicillin and corticosteroid therapy is indicated. Drug-induced vasculitis should be treated by cessation of the incriminated drug. With cases of suspected photoactive vasculitis, exposure to the sun should be minimized, and the use of antiinflammatory drugs as well as sunscreen on exposed nonpigmented skin is recommended.

Supplemental Readings

- Brianseau P, Divers TJ: Acute thrombosis of limb arteries in horses with sepsis: five cases (1988-1998). *Equine Vet J* 2001; 33:105-109.
- Carr EA, Carlson GP, Wilson WD et al: Acute hemorrhagic pulmonary infarction and necrotizing pneumonia in horses: 21 cases (1967-1993). *J Am Vet Med Assoc* 1997; 210:1774-1778.
- Clare AC, Kraje BJ: Use of recombinant tissue-plasminogen activator for aortic thrombolysis in a hypoproteinemic dog. *J Am Vet Med Assoc* 1998; 212:539-543.
- Rijkenhuizen AB, Van Swieten HA: Reconstruction of the jugular vein in horses with post thrombophlebitis stenosis using saphenous vein graft. *Equine Vet J* 1998; 30:236-239.
- Ross MW, Maxson AD, Stacy VS et al: First-pass radionuclide angiography in the diagnosis of aortoiliac thromboembolism in a horse. *Vet Radiol Ultrasound* 1997; 38:226-230.
- Saville WJ, Hinchcliff KW, Moore BR et al: Necrotizing enterocolitis in horses: a retrospective study. *J Vet Intern Med* 1996; 10:127-132.
- Triplett EA, O'Brien RT, Wilson DG et al: Thrombosis of the brachial artery in a foal. *J Vet Intern Med* 1996; 10:330-332.
- Venco L, Calzolari D: Pulmonary thromboembolism in a dog with renal amyloidosis. *Vet Radiol Ultrasound* 1998; 39:564-565.
- Welch RD, Dean PW, Miller MW: Pulsed spectral Doppler evaluation of a peripheral arteriovenous fistula in a horse. *J Am Vet Med Assoc* 1992; 200:360-362.

SECTION XII

Foal Diseases

Edited by Dr. Elizabeth A. Carr

CHAPTER 12.1

Evaluation and Early Care of the Sick Neonatal Foal

KIM A. SPRAYBERRY

Lexington, Kentucky

ELIZABETH A. CARR

East Lansing, Michigan

Few areas of equine medicine have advanced in the last two decades as much as neonatal intensive care. Neonatal intensive care units (NICUs) are present in almost every major veterinary school, and many private referral centers now operate NICUs in their individual hospitals. Many foals once considered to have a poor prognosis are now treated successfully and discharged from such facilities. Although the survival numbers have improved dramatically, the cost of treatment has likewise continued to increase, and expense considerations significantly affect owners' decisions about treatment plans and options. Consequently, it is important to identify those risk factors and physical parameters that suggest that a foal is ill or at risk for illness, in addition to those factors that ultimately may affect the prognosis for both athleticism and life.

This information aids the owner in reaching an informed decision as to whether or not a particular compromised foal should be treated. Once a decision is made to treat, using available technology to identify problems in their earliest stages, including in the prepartum period, permits earlier intervention and maximizes the likelihood that the emotional and financial investment in the foal will lead to a favorable outcome. The purpose of this chapter is to define and discuss the information in a foal's history, including prepartum conditions and the parturition process, its physical exam, and the results of adjunctive diagnostic tests that are associated with an increased likelihood of illness and which may indicate that the neonate should be referred to a secondary care center.

PREPARTUM MATERNAL SIGNS OF FETAL COMPROMISE

Although the majority of mares have an uneventful gestation and foal successfully with little, if any, intervention, in other mares, premonitory signs, either present as a clinical finding during physical examination or as a component of the history, warrant additional scrutiny for potential problems. Mares that have had complications such as endometritis, dystocia, abortion, or a foal affected by neonatal isoerythrolysis in the past are obvious candidates for an escalated degree of observation. Maiden mares also warrant a higher degree of surveillance because they may be less likely to demonstrate obvious mammary development or other signs of impending parturition. Known causes of late-term fetal loss include the presence of twins; viral infections such as equine herpes I and equine arteritis virus; bacterial infections such as leptospirosis; placentitis resulting from bacterial, mycotic, and nocardioform etiologies; endometrial insufficiency; poor nutrition; umbilical cord strangulation; and uterine hydrops. Severe maternal illness conditions such as endotoxemia, fever, cardiovascular disease, renal failure of advanced pregnancy, prepartum uterine artery hemorrhage, or conditions requiring general anesthesia and surgical intervention also may lead to compromise and loss of the fetus.

Although some of the above conditions can result in abortion without premonitory warning signs, clinical signs that point to the impending termination of the pregnancy accompany others. The presence of vaginal discharge and premature lactation are the most common

indications that the pregnancy and fetus are at risk. Mares carrying twin fetuses typically demonstrate premature mammary development and lactation, whereas mares with placentitis frequently develop these signs plus purulent vaginal discharge. Purulent vaginal discharge in pregnant mares is the principal sign of placentitis. In such cases a vaginal speculum exam should be performed, the appearance of the cervix noted, and any discharge present cultured.

After rectal palpation to ascertain uterine tone and volume, imaging with ultrasound should be employed to assess the condition of the fetus and to visualize the uterine and placental tissues. Transrectal imaging may demonstrate thickening or separation of the placenta in the area of the cervical star, indications that infection has reached the uterus via an ascending route. Transabdominal ultrasonography is used to assess the ventral portions of the uterus and placenta. The combined thickness of the uterus and placenta can be determined and areas of placental edema, infiltration, or separation from the endometrium identified. The normal thickness of the combined uterine wall and chorioallantoic membrane is 0.6 to 1.5 cm.

Abnormal findings in the ventral portion of the uterus without changes at the cervical star are thought to arise from either hematogenous bacterial distribution or organisms present at conception. Multifocal or diffuse areas of placental separation result in reduced exchange of nutrients and oxygen, resulting in chronic oxygen deficit. These foals are frequently born with signs of hypoxic ischemic encephalopathy (HIE) even when the actual process of delivery takes place promptly and birth asphyxia per se is not a complicating factor. The sonographic detection of significant placental separation is grounds for the additional concern of premature placental separation during delivery. The notation of any of these uterine wall abnormalities signifies a high-risk pregnancy, and indicates the need for intervention and close observation.

In addition to the uteroplacenta, many features of the fetus can be assessed with transabdominal ultrasound, including the heart rate, aortic diameter, activity levels, and appearance of the placental fluids. Normal fetal heart rate in late gestation is in the range of 60 to 120 bpm; sustained rates below or above this range are an indication of fetal compromise. Diagnostic transabdominal images of the uteroplacental wall can be obtained with both linear array and sector transducers. A 5.0- or 7.5-MHz probe delivers the best detail for imaging of the uteroplacenta, whereas the longer-wavelength 2.5- to 3.5-MHz sector transducers are best for imaging fetal structures, especially larger fetuses in the latter stages of gestation.

Bloody vulvar discharge is frequently a result of varicose vessels in the vaginal walls, particularly in the area of the remnant transverse fold and would not be expected to interfere with pregnancy unless significant anemia has resulted from chronic blood loss. These vessels can be ligated if necessary but regresses naturally after parturition.

Placental fluids that are echogenic or contain gas echoes may be an indicator of illness in the fetus, although the late-gestation presence of flocculent or cellular allantoic fluid, in the absence of other abnormalities, may be normal. Excessively voluminous allantoic fluid viewed on ultrasound and an inability to ballot the fetus during rectal

palpation because of the surrounding fluid are hallmarks of hydrops allantois. Hydrops amnii also has been reported but is rare in mares. Viable foals rarely result from either hydrops amnion or hydrops allantois, and the excessive weight of the fluid and fetus predisposes mares to compromised prepubic tendon integrity and possible rupture. Identification of this abnormality should prompt efforts to either sequentially remove a portion of the fluid or terminate the pregnancy. These procedures often justify referral to a clinic because the hemodynamic consequences of abrupt removal of the third-space fluid volume can be severe and have been associated with shock, collapse, and death of the mare. Induction of parturition in these cases may result in dystocia because of uterine inertia brought about by prolonged stretching of the myometrium.

Prepartum Treatment

Treatment with broad-spectrum antimicrobial drugs should be instituted in pregnant mares with vaginal discharge if a heartbeat or other signs of fetal viability are present. Live foals can be recovered from mares with placentitis or *in utero* infections, but treatment with antibiotics generally is recommended for the remainder of gestation. Antiinflammatories such as flunixin meglumine, agents such as the antiinflammatory and hemorrhheologic drug pentoxifylline, tocolytics such as clenbuterol, and endocrine supplementation of progesterone or progestagens, also may be considered. When placentitis develops after gestation has reached 300 days, the chances for saving the foal are improved, although it is crucial to assume that the foal will be infected or septicemic at birth and institute treatment accordingly. The postpartum survival of foals born under such circumstances actually may be enhanced by the sustained intrauterine immune challenge and activation of the hypothalamus-pituitary-adrenal axis and stress-hormone release. Aggressive broad-spectrum antibiotics and rigorous monitoring during the remainder of gestation are indicated, and treatment for sepsis should be instituted at birth, without waiting for results of blood culture or other clinicopathologic confirmation of sepsis. Identification of a high-risk foal with sonographic fetal monitoring permits planning for treatment on the farm or referral to a hospital. Referral of the mare to the hospital before foaling may be advantageous; once delivery has occurred, aggressive supportive care for a sick neonate can be instituted immediately.

Premature lactation and the dripping of milk are concerns because of the potential for loss of colostrum and subsequent failure of passive transfer. Normally the mammary gland undergoes final enlargement and the commencement of lactation during the last few days to a week preceding parturition. Owners of mares that demonstrate inappropriately early udder development and lactation should be advised to obtain an alternate source of colostrum and keep it on hand so that it can be thawed and administered to the foal. In general, good quality colostrum is thick, sticky, and yellowish in color.

Accurate determination of colostrum quality can be performed directly by determining its immunoglobulin concentration or indirectly by measuring the specific gravity with a colostrometer (Jorgensen Labs, Inc., Loveland,

Colo.). It has been suggested that colostrum with a specific gravity of 1.06 or greater contains satisfactory levels of immunoglobulin. If equine colostrum is not available, bovine colostrum may be used, although the half-life of bovine immunoglobulin in the foal is short. Chapter 12.13 provides further discussion of colostrum replacements and assessment the adequacy of passive transfer.

Although mares that have not foaled within a week of the calculated due date are a source of anxiety to many owners, approximately 14 days plus or minus the mean (341 days) gestation length would be considered within normal range for any individual. Gestational length alone is not a dependable indicator of fetal readiness for birth. Prolonged gestation in a mare may be a normal variation or may be due to delayed fetal maturation, such as occurs from grazing *Acremonium*-infected fescue forage. In general, induction of delivery is not recommended unless ultrasound monitoring has detected some condition (severe placentitis, severe placental separation, sonographic signs of fetal stress or fading) that suggests that the near-term fetus is unequivocally better off outside the uterine environment than inside it.

The occurrence of any serious illness in the pregnant mare constitutes a risk factor for fetal or neonatal problems. In mares whose value justifies the expense, an episode of serious disease, even if transient, provides ample grounds for recommendations to the owner for more detailed surveillance, including serial blood and ultrasound monitoring. Overt external signs such as vaginal discharge or premature lactation are red flags for an at-risk pregnancy and a compromised fetus. Mares with placentitis are rarely systemically ill.

SIGNS OF PROBLEMS DURING PARTURITION AND IN THE IMMEDIATE POSTPARTUM PERIOD

The foaling process is rapid, with the second, or expulsion, phase of parturition being completed within about 30 minutes of rupture of the chorioallantoic membrane. Prolongation of this phase of the delivery leads to asphyxiation and/or death of the foal. Given the narrow window of time for intervention with dystocia, owners must be educated regarding the expected pace of the normal foaling process. A helpful rule of thumb for owners is that every 10 minutes in the delivery process should bring about significant progress in the foal's expulsion, and prompt veterinary intervention should be summoned if not noted. Premature placental separation, or so-called "red bag" delivery, also leads to asphyxiation, and owners should be counseled on how to recognize this complication and to tear the membrane and deliver the foal as promptly as possible. If placental separation commenced during the earlier stages of labor, the foal may suffer from hypoxia even if the abnormal presentation is recognized and dealt with as soon as the velvety, red chorionic villosa surface appears at the vulva. Foals that experience deliveries complicated by premature placental separation should be monitored closely for behavioral abnormalities associated with HIE. An increased risk of premature placental separation is seen in late gestation mares in which significant areas of placental separation have been identified sono-

graphically in addition to mares undergoing induction of parturition. The latter association is thought to be due to the powerful myometrial contractions induced by administration of exogenous oxytocin.

Meconium staining or so-called fetal diarrhea is manifested by icteric to green discoloration of the amnion and/or yellowish staining of the skin and mucous membranes of the foal. This complication is an indication of fetal distress during late gestation or parturition and should prompt detailed assessment of the foal, including sonographic imaging to assess for pneumonia secondary to aspirated meconium, gastrointestinal disease, or other abnormal conditions. These foals should be assumed to be ill and should be treated with broad-spectrum antibiotics.

THE NEONATAL FOAL

Normal parameters have been established for neonatal foal behaviors, and departure from these recognized norms should be interpreted as risk factors. A newborn foal should be able to right itself within moments of birth, stand within 2 hours and be nursing soon afterward. Musculoskeletal abnormalities, including contracted or lax tendons, that result in difficulty standing and a resultant delayed or inadequate nutritional intake should be addressed as soon as identified to prevent hypoglycemia and septicemia.

Tube Feeding

If the foal cannot be assisted adequately to stand and nurse, placement of an indwelling stomach tube and feeding of colostrum are required. Given the rapidity with which hypoglycemia can develop, foals must be fed on a regular hourly or bihourly schedule. A normal foal requires approximately 15% of its body weight in milk over a 24-hour period for maintenance requirements. For example, a 45-kg foal should ingest 6.75 L of milk over a 24-hour period, and if being fed every 2 hours through an indwelling nasogastric tube, should be given about 560 ml at each feeding. This does not take into account additional needs for growth or the increased metabolic rate associated with illness such as sepsis.

In sick foals, it is prudent to start with a smaller volume (10% of body weight/24 hours) and gradually increase the amount fed hourly, checking for reflux, signs of discomfort, or other indications that the volume being fed is not being tolerated. Because healthy foals nurse small amounts frequently (30-second to 3-minute episodes as frequently as four to eight times an hour), the feeding of larger volumes every hour or two can result in colic, reflux, and diarrhea, particularly in the septic or premature foal with decreased bowel motility and digestive function. A foal that does not stand and nurse unassisted should be assessed further for underlying sepsis or HIE once it has been instrumented for nutritional support.

Sepsis and Hypoxic-Ischemic Encephalopathy

Foals with sepsis or hypoxic-ischemic encephalopathy (HIE) may appear normal at birth, gradually losing the normal suckle reflex and becoming lethargic and less

responsive over the first 12 to 48 hours of life. Attendants should observe carefully the attempts to nurse because ill or maladjusted foals may stand under the mare, make suckling noises, and appear to nurse without actually grasping the teat and ingesting milk. Evaluation of the mare's udder and daily weighing of the foal are simple ways to assess milk intake and well being. A light horse foal should gain between 1 and 2 pounds every day.

Engorgement of the mare's udder and the appearance of "milk face" on the foal (milk running down the forehead or face) should be interpreted as signs of trouble. If early, subtle signs are not detected, dehydration and other complications develop. It is inappropriate to address weakness or fading in a newborn foal by simply supporting the functions that the foal is unable to perform, like helping a foal to rise or instructing owners to bottle feed milk into the mouth of a foal with a poor suckle reflex. Such foals are likely to be compromised by birth asphyxia and/or septicemia, and the apparent weakness and slow start are merely signs of a much more serious primary problem.

Septicemic foals may have normal bursts of activity, especially when restrained for examination, but their overall level of activity is decreased. When closely scrutinized, evidence of dehydration, injected membranes, diarrhea, or other clinical findings are usually evident. Typical clinical findings suggestive of sepsis include injected mucus membranes, petechial hemorrhages of the sclerae and ears, fever, lethargy, depression, and partial to complete anorexia. A foal exhibiting any of these signs should be assumed to be ill and undergo further diagnostic testing.

Premature Foals

Premature foals typically have a low birth weight and demonstrate features associated with incomplete physical maturation. Foals that are septicemic or suffering the effects of birth asphyxia may appear normal in body size and external features but are behaviorally or neurologically deficient. Because it is difficult to distinguish between a newborn foal that is weak because of sepsis from one that has suffered only from birth asphyxia, and because many foals are affected by both problems, proper treatment of any compromised foal should include broad-spectrum antimicrobials. Premature foals, foals overtly ill at delivery, and those that appear normal at birth but fade afterwards should be assumed to be septic or highly at risk for sepsis and accordingly have a complete physical examination and blood work, including blood cultures, performed. A positive blood culture is proof that septicemia exists, but a negative result does not rule out its presence. That fact, together with the 48- to 72-hour lag time before results are known, makes it inadvisable to withhold treatment for sepsis until blood culture results become available.

The basic database desired for compromised foals includes a complete blood count (CBC), fibrinogen, serum chemistry especially electrolytes, HCO_3^- , glucose, bilirubin, renal parameters, liver enzymes, serum IgG concentration, and blood culture. Arterial blood gas analysis also should be ordered if indicated by respiratory stress or cyanotic mucous membranes. Changes in the CBC that should prompt suspicion of sepsis include leukopenia, neutropenia, and a left shift. Such findings, along with other metabolic derangements including dehydration, azotemia,

electrolyte imbalances, and metabolic acidosis, are justification for institution of a treatment plan, serial monitoring, and possible referral to a secondary care center.

Ischemia and bacteremia resulting from sepsis and hypoperfusion can result in gastrointestinal damage, diarrhea, ileus, and colic, and subsequent derangement of serum electrolytes. Such findings also can be an indicator of a primary infection with an enteric pathogen. The reality in regard to a neonate is that treatment of both diseases is similar, consisting of broad-spectrum antibiotics, volume resuscitation, and supportive care. Elevation of serum creatinine in the newborn foal can be an indicator of placental insufficiency and should alert the clinician to possible *in utero* compromise. Elevations in serum creatinine should decrease steadily to normal values over the first 3 to 5 days in the absence of primary renal disease. Renal and abdominal ultrasound in addition to a urinalysis are indicated to rule out other causes of azotemia including congenital renal anomalies, uroperitoneum resulting from a ruptured bladder or urachus, pyelonephritis, or other renal damage secondary to septicemia or ischemia. Ultrasound imaging can be used as an extension of the physical exam in foals and effectively demonstrates a variety of abnormal conditions in the heart, thorax, abdomen, and umbilical structures. Radiography or ultrasound can be used to examine the lungs and ribs. A sepsis score may be derived from laboratory and physical exam parameters and combined with blood culture results to aid in predicting sepsis; however, it should be stressed that the compromised, at-risk newborn should be treated even if the sepsis score or other test results are equivocal.

A preemptive approach to therapeutic intervention is valid for several reasons. From the beginning foals are more susceptible to illness. Even with adequate colostrum intake their immune systems are not fully developed; consequently, their response to infection may be lacking. Their higher metabolic rate and greater surface area-to-body mass ratio make them more susceptible to dehydration, hypothermia, and inadequate nutritional support. Their lack of body stores and compensatory metabolic mechanisms result in development of hypoglycemia, hypothermia, and metabolic acidosis much more rapidly than the adult horse. In addition, it is easy to miss the severity of illness in the periparturient period. A septicemic foal initially may manifest signs of being slightly sleepy or mildly inappetent. Many septic foals have subnormal to normal body temperatures consequently, many of the signs clients associated with infection are not helpful in the neonate. Consequently, close monitoring of the early neonatal period, particularly when problems have been identified previously during gestation or parturition, is critical in detecting the onset of illness and ensuring intervention at the earliest moment.

PROGNOSTIC FACTORS IN COMPROMISED NEONATAL FOALS

Hospitalizing a sick foal may increase significantly the chances for a favorable outcome, but the costs for such care should be anticipated, explained to the owner, and considered in light of the severity of the foal's condition, likelihood for survival, and presence of congenital problems that may preclude future athletic utility. Ill foals born with concurrent congenital cardiac defects or ophthalmic

abnormalities, for example, may survive sepsis or HIE with supportive care and treatment but have a low probability for performing athletically in the future. Premature or dysmature, septicemic foals may be treated successfully for their primary problem but develop juvenile osteoarthritis and chronic lameness as a result of damage to the incompletely ossified, small bones of the hocks and carpi.

No laboratory test or specific physical exam finding can predict accurately the response to treatment or eventual outcome in a compromised foal. However, trends in clinical signs and laboratory tests observed after several days of supportive care are helpful in determining the likelihood of successful treatment. In general, the lower the gestational age and weight at birth, the greater the severity of medical problems and attendant complications. Foals delivered at 300 days of gestation and earlier may survive with an aggressive and sometimes protracted course of care but are at high risk for complicating problems. In each case, the foal's owner should be queried as to whether the foal's genetic profile makes salvage for breeding a reasonable goal, what the medical budget limitations are, and how much of the intensive nursing effort and medical expertise can be provided at the farm if referral to a secondary care center is not possible.

DECISION TO REFER TO A SECONDARY CARE FACILITY

The owner, caretaker, and attending veterinarian are the concerned parties when the question arises of whether or not to refer the foal for additional care. In addition, claims adjustors or other insurance company representatives must be involved with and informed of decisions regarding insured foals. The latter situation is growing more common and makes the delivery of an increased level of veterinary care available to a greater number of horses but necessitates excellent communication between the owner, adjustor, and veterinarians.

CARE OF THE FOAL DURING TRANSPORT

The rapid increase in knowledge and expertise in equine neonatal medicine has greatly augmented the veterinarian's ability to save even severely compromised foals. When the decision is reached to refer the foal for hospitalization and intensive care, several supportive measures can be provided before shipping that stabilize the foal's condition during transit. Foals that are hypothermic and otherwise showing signs of septic shock, for example, should receive an initial dose of glucose-containing intravenous fluids and be administered 500 ml colostrum through a nasogastric tube. Warming the foal is essential and can be facilitated by wrapping in blankets or restraining the foal in the back seat of a pickup or van during transit. Helping the newborn maintain a sternal body position is also advantageous. If the referral center is more than a few hours' drive away, the referring veterinarian should consider aseptically collecting blood and inoculating culture bottles to send with the foal and initiating antibiotic treatment before departure. These measures, plus making the decision to refer the foal earlier rather than later in the course of events, enhance the likelihood of the neonate's survival.

In summary, routine pregnancy and fetal monitoring are helpful in assessing fetal well-being in any mare but are especially indicated in mares with a history of periparturient problems or which are showing clinical signs of vaginal discharge or premature lactation. If examination, imaging, and/or bloodwork demonstrate fetal compromise, treatment can be instituted while the foal is still *in utero*, and an appropriate course of action can be planned for the anticipated problems at birth. After delivery, foals should be assessed closely for normal behavioral and blood profile parameters, and any departures from normal should be interpreted as an indication for increased surveillance and serial monitoring and for the provision of antibiotics and other supportive measures as indicated. If the anticipated care measures cannot be provided adequately by the owner, the question of whether to refer the foal to a NICU arises and should be considered in light of cost estimates from the referral facility, regard for the foal's value, the severity of its condition, and the presence of concurrent conditions such as musculoskeletal or cardiovascular problems that would affect the prognosis for survival and usage potential.

Supplemental Readings

- Adams R, Poulos PW: Skeletal ossification index for neonatal foals. *Vet Radiol* 1988; 29:217.
- Brewer BD: Identification and early management of the high-risk neonatal foal. In Robinson NE (ed): *Current Veterinary Therapy in Equine Medicine*, 3rd edition, pp 411-414, Philadelphia, WB Saunders, 1992.
- Geor R: Clinical evaluation and early management of the abnormal neonate. In Kobluk CN, Ames TR, Geor RJ (eds): *The Horse: Diseases and Clinical Management*, p 1209, Philadelphia, WB Saunders, 1998.
- Koterba AM: Diagnosis and management of the normal and abnormal neonatal foal: general considerations. In Koterba AM, Drummond WC, Kosch PC (eds): *Equine Clinical Neonatology*, p 3, Philadelphia, Lea & Febiger, 1990.
- Koterba AM: Acute and chronic asphyxia in the neonate. In Smith BP (ed): *Large Animal Internal Medicine*, p 313, St Louis, Mosby, 1990.
- Koterba AM, Brewer BD, Tarplee FA: Clinical and clinicopathological characteristics of the septicemic neonatal foal: review of 38 cases. *Equine Vet J* 1984; 16:376-382.
- Lavoie JP, Spensley MS, Smith BP et al: Absorption of bovine colostral immunoglobulins G and M in newborn foals. *Am J Vet Res* 1989; 50:1598-1603.
- LeBlanc MM, McLaurin BI, Boswell R: Relationship among serum immunoglobulin concentration in foals, colostral specific gravity, and colostral immunoglobulin concentration. *J Am Vet Med Assoc* 1986; 189:57-60.
- Paccamonti DL: Abortion. In Kobluk CN, Ames TR, Geor RJ (eds): *The Horse: Diseases and Clinical Management*, p 1013, Philadelphia, WB Saunders, 1998.
- Reef VB: Fetal ultrasonography. In Reef VB: *Equine Diagnostic Ultrasound*, pp 425-445, Philadelphia, WB Saunders, 1998.
- Santschi EM, LeBlanc MM, Matthews PM et al: Evaluation of equine high-risk pregnancy. *Comp Cont Educ Pract Vet* 1994; 16(1):80-87.
- Santschi EM, LeBlanc MM: Fetal and placental conditions that cause high-risk pregnancy in mares. *Comp Cont Educ Pract Vet* 1995; 17(5):710-720.
- Vandeplasse M, Bouters R, Spincemille M: Dropsy of the fetal sacs in mares: Induced and spontaneous abortion. *Vet Rec* 1976; 99:67-69.

CHAPTER 12.2

Neonatal Isoerythrolysis

JAMI L. WHITING
Dubai, United Arab Emirates

Neonatal isoerythrolysis (NI) is an immunologic disease of the newborn foal, characterized by clinical signs consistent with hemolytic anemia. In cases of NI, the foal inherits a specific red blood cell (RBC) surface antigen from the sire, which is incompatible with antibodies present in the colostrum of the dam. After ingestion, absorbed antibodies bind to the foal's RBC, which results in hemolysis and consequent anemia. The prognosis for NI is variable and depends upon the amount and type of sensitizing antibody, the rapidity and the severity of hemolysis, and the time course to detection and treatment of the foal.

Eight equine blood groups have a total of 32 distinct RBC antigens. Of these antigens, Aa and Qa account for the majority of cases of NI. The RBC antigens Pa, Ab, Dc, Db, Qc, and Ua are less commonly implicated in cases of equine NI. Aa and Qa antigens appear to be the most antigenic, which may account for their higher incidence in inducing NI. The prevalence of the Ca antigen within a population appears to influence the incidence of NI. Mares that are Ca-negative frequently produce Ca antibodies but rarely produce a foal affected with NI. Ca antibodies actually may prevent sensitization of the mare to Aa antigens via antibody-mediated immunosuppression.

The mare begins to produce antibody after exposure and sensitization to incompatible RBC antigens. Sensitization can occur when mares receive blood transfusions or homologous tissue vaccines. More commonly, exposure to incompatible RBC antigens occurs during transplacental hemorrhage late in gestation or placental hemorrhage during parturition. Although mares can become exposed and generate antibody during any pregnancy, primiparous mares rarely give birth to NI-affected foals because transplacental hemorrhage during this first pregnancy fails to stimulate an immune response of sufficient strength. Once a mare has had an NI foal, however, all future pregnancies are at risk.

Neonatal isoerythrolysis is more common in mule foals than in horse foals. All donkey RBCs have a unique donkey antigen not present in horses. Given the fact that not every mule foal develops NI, additional unrecognized factors may influence the incidence of the disease in the mule.

CLINICAL SIGNS

Affected foals are typically normal at birth. Clinical signs develop after ingestion and absorption of colostrum, with onset of signs occurring anywhere from 5 hours to 5 days of age. Clinical signs vary depending on the rate of he-

molysis in addition to the severity of the resulting anemia. Cases with gradual onset and/or mild anemia simply may exhibit an increased respiratory rate and signs of lethargy. Any abnormal behavior or activity in a foal should warrant a closer exam and will likely reveal tachycardia and evidence of pale, icteric mucous membranes. Foals in which the anemia is more profound, or develops rapidly, frequently show evidence of depression, partial anorexia, dehydration, pale, icteric mucous membranes in addition to tachypnea, tachycardia, pigmenturia, and not infrequently, fever. In peracute, or severe cases, cardiovascular collapse, and hemodynamic shock resulting from hypoxia can result in neurologic disorders, metabolic acidosis, and multiorgan failure. Progression of clinical signs may be rapid and death may occur within hours, even before the appearance of icterus. Compromised foals are at high risk for developing secondary problems such as septicemia. Fevers can result from the inflammatory response to hemolysis or secondary to sepsis. Kernicterus (bilirubin encephalopathy) has been reported in NI foals and is attributed to the neurotoxic effects of high levels of circulating unconjugated bilirubin.

Differential diagnoses for a weak neonatal foal with icterus include septicemia, hypoxic-ischemic encephalopathy (NMS/HIE), equine herpesvirus 1 (EHV-1), anemia of prematurity, folate insufficiency, coagulopathies, toxin ingestions, and disseminated intravascular coagulopathy. Other causes of anemia in the neonate include hemothorax/hemopericardium secondary to rib fractures, vascular accidents involving umbilical structures leading to hemoperitoneum or external hemorrhage, or idiopathic hemoperitoneum.

DIAGNOSIS

The primary clinicopathologic abnormality in a foal with NI is anemia. Extravascular hemolysis is the primary mechanism of erythrocyte removal, but intravascular hemolysis may occur. Other clinicopathologic abnormalities include hyperbilirubinemia (primarily the unconjugated form) and hemoglobinuria. Mule foals commonly develop thrombocytopenia in addition to anemia. Azotemia can occur as a result of the nephrotoxic effects of hemoglobin on renal tubular cells in addition to dehydration because of lethargy and decreased milk intake.

Metabolic acidosis as a result of tissue hypoxia may occur with severe or rapid hemolysis. In foals that are too weak to stand and nurse adequately, hypoglycemia and dehydration frequently develop. Hematology may demonstrate sepsis, with either an increased or decreased white blood cell count coupled with an increased fibrinogen.

Laboratory confirmation of NI requires demonstration of antibodies (maternally derived) that bind the foal's RBCs. Cross-matching tests, including hemolytic and agglutination assays, are the most commonly used tests. The agglutination assays may not detect all sensitizing antibodies because some antibodies act as hemolysins; consequently assays for hemolytic antibodies are more sensitive. In testing for hemolytic antibody serum from the mare is mixed with RBCs. If hemolytic antibody is present, RBC lysis occurs after the addition of complement. The requirement of an exogenous source of complement limits the availability of this test.

The jaundice foal agglutination (JFA) test is a cross-match test that does not require the use of complement (Box 12.2-1). The JFA test requires a centrifuge and minimal laboratory items and is easily performed by the attending veterinarian. Serial dilutions of the mare's colostrum are mixed with the foals RBCs, placed in test tubes and centrifuged. Centrifugation of the mixture allows the cells to come into close proximity with NI antibodies and enhances agglutination.

The hemolytic and the JFA tests are predictive for NI when performed prior to ingestion of colostrum. After absorption of colostrum, both tests are subject to misinterpretation since agglutination and/or lysis of RBC may have occurred already.

The positive direct antiglobulin test (Coombs' test) can be used to demonstrate the presence of antibodies or complement bound to the foal RBCs; however, it is not specific for NI.

PREVENTION

A flow diagram (Figure 12.2-1) is given describing the type and timing of testing to best ensure detection of individuals at risk for NI before foaling. Early detection of individuals at risk allows enough time to identify an alternative source of colostrum in preparation for foaling.

Mares that test negative for Aa, Qa, Ua, or Pa should be considered at risk for making NI antibodies and stallions bred to these mares blood-typed to determine if they are positive for the specific RBC antigens. If the stallion tests positive, the mare's serum should be screened for the presence of anti-RBC antibody approximately 30 days before foaling. Testing should be repeated closer to the time of foaling when suspicious results are obtained from the first screening test. If results of screening are positive an alternative colostrum source needs to be located. If a mare has demonstrated serologic evidence of anti-RBC antibodies a hemolytic test or a JFA test should be performed on the foal immediately post foaling and before nursing to definitively identify foals at risk for NI.

BOX 12.2-1

Jaundice Foal Agglutination (JFA) Test

Materials

- Centrifuge capable of spinning 300 to 600 times gravity
- Test tube rack
- Test tubes: 13 × 100 mm disposable tubes or blood collection tubes (red-topped tubes, no anticoagulant)
- Pasteur pipettes and rubber bulbs or other pipette system to deliver 1 ml volumes
- Isotonic (0.9%) saline at room temperature
- Serum or colostrum from the mare; red blood cells from the mare and foal preferably in EDTA anticoagulant (purple-topped tubes)

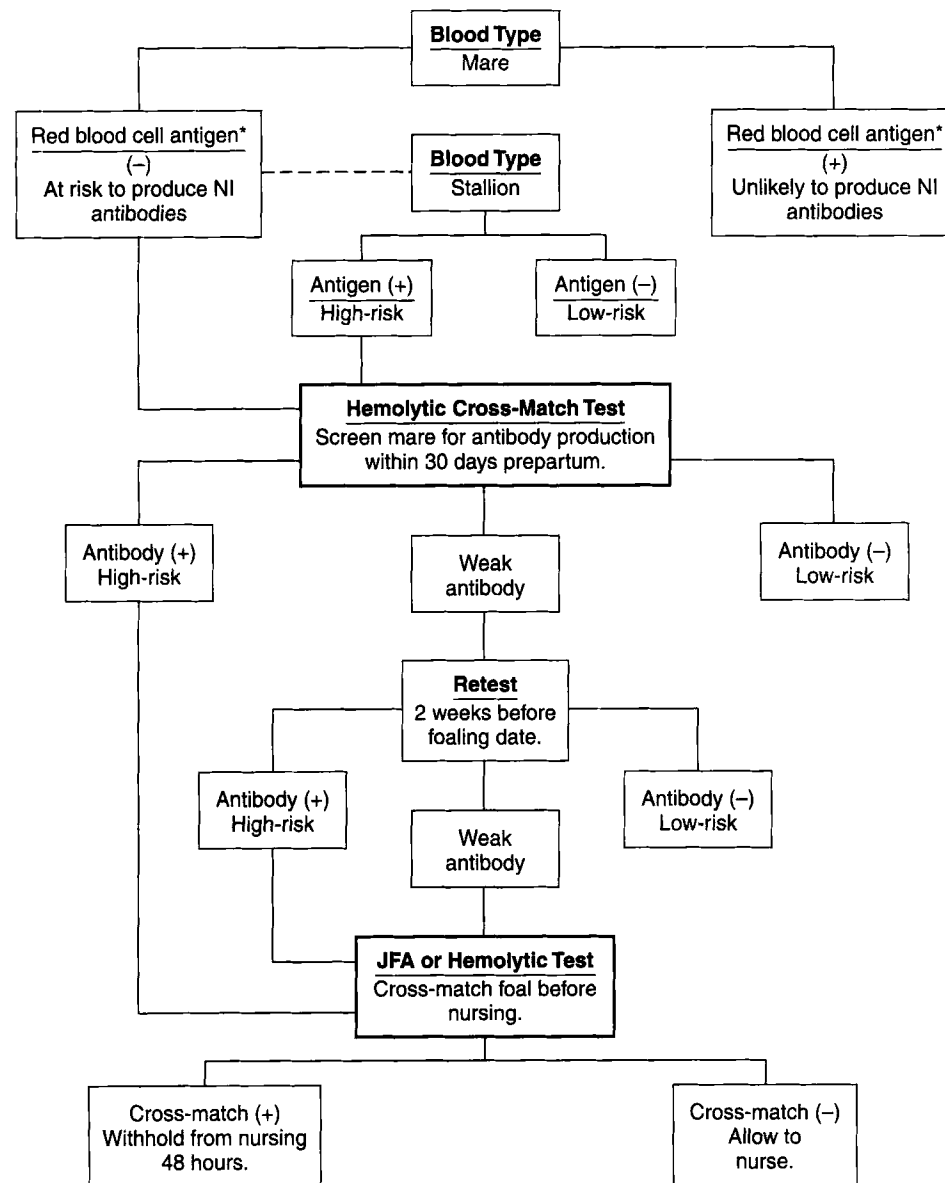
Method

1. Collect colostrum or serum from the mare.
2. Collect a blood sample from the foal before it nurses in an EDTA (purple-topped) anticoagulant tube.
3. Add 1 ml of saline to each of six tubes. Label the tubes: Control, 1:2, 1:4, 1:8, 1:16, and 1:32.
4. Make serial dilutions of the mare's colostrum (or serum) at 1:2, 1:4, 1:8, 1:16, and 1:32 by adding 1 ml of colostrum (or serum) to the tube labeled 1:2 and mix, then take 1 ml from that tube and add it to the tube labeled 1:4 and mix. Continue the process until all five dilution tubes are prepared. Discard 1 ml from the tube labeled 1:32.
5. Add one drop of the foal's whole blood to each of the six tubes and mix.

6. Centrifuge the tubes for 2 to 3 minutes at a medium speed (300-600 times gravity).
7. Invert each tube, pour out the liquid contents and observe the status of the "button" of agglutination at the bottom of the tube. Complete agglutination causes the cells to remain tightly packed to the button, whereas strong agglutination causes the cells to form large clumps. When agglutination is weaker, cells are in smaller clumps as they run down the sides of the tube; when no agglutination occurs, the cells flow easily down the sides of the tube (this is what should happen in the control tube). If cells clump in the control tube, they may be auto-agglutinating and the results are questionable.
8. If a positive reaction occurs with the foal's cells, the test should be performed using the dam's own red blood cells to ensure that neither the conditions of the test nor the viscosity of the colostrum is causing the agglutination.
9. Positive reactions at dilutions of 1:16 or greater are considered significant; at these dilutions, this test correlates well with the standard hemolytic assay. Correlation is not as good at lesser dilutions and more false-positive results will occur. Other factors (e.g., the viscosity of the colostrum) also can make less-diluted samples more difficult to read.

EDTA, Ethylenediaminetetraacetic acid.

NEONATAL ISOERYTHROLYSIS TESTING



*Red blood cell antigens refer to those antigens known to cause NI in foals (e.g., Aa, Qa, Pa, Ua, Db, Dc, and Ab).

Figure 12.2-1 Neonatal isoerythrolysis (NI) testing.

Foals with a positive JFA test or hemolytic test should be muzzled for a period of 30 to 48 hours postpartum. The mare's udder should be stripped at 2-hour intervals to remove all colostrum and to maintain milk production. The foal should receive the alternative colostrum within the first few hours of life (negative for anti-RBC antibodies) to prevent failure of passive transfer and should subsequently be fed milk replacer until removal of the muzzle. In some situations, it may be most effective to pass a nasogastric tube to ensure adequate and timely ingestion of colostrum. Foals reluctant to nurse from a bottle should not be forced because the risk for aspiration is high. These foals should be fed via a nasogastric tube until the muzzle can be safely removed. The foal's serum IgG level should be determined at 12 to 24 hours of age to assess transfer of immunoglobulins. If the alternative colostrum source fails to supply adequate immunoglobulins plasma transfusion is recommended.

Many farms maintain a colostrum bank for immediate use when required. Colostrum should be tested for anti-RBC antibodies and only those negative for high risk antibody should be stored. See Box 12.2-2 for a list of laboratories that perform testing.

TREATMENT

The foal's clinical signs in addition to the severity of the anemia determine the need for transfusion. Foals with mild anemia (PCV greater than 15%) that are reasonably active and nursing adequately may not require a transfusion and may be managed with stall confinement to limit stress and exercise. Blood product transfusions and supplemental oxygen therapy should be considered strongly in foals exhibiting more severe clinical signs including weakness, tachypnea, fevers, neurologic signs, dehydration, and

BOX 12.2-2

Laboratories Providing Diagnostic Services for Equine Neonatal Isoerythrolysis***Veterinary Genetics Laboratory†**

School of Veterinary Medicine
University of California—Davis
Davis, CA 95616
530-752-2211

Stormont Laboratories, Inc.†

1237 East Beamer Street, Suite D
Woodland, CA 95776
590-661-3078

Hagyard-Davidson-McGee Laboratory

4250 Iron Works Pike
Lexington, KY 40511
859-259-3685

Equine Blood Typing and Research Laboratory†

Department of Veterinary Science
University of Kentucky
Lexington, KY 40546
859-257-3022

Rood & Riddle Equine Hospital

2150 Georgetown Road
Lexington, KY 40511
859-233-0331

Shelterwood Laboratories†

P.O. Box 215
Carthage, TX 75633
903-693-6424

Maxxam Analytics†

335 Laird Road, Unit 4
Guelph, ON N1H 6J3
Canada
519-836-2400

Veterinary Laboratory, Inc.

1033 North Limestone
Lexington, KY 40505
859-252-0415

*Serum and/or colostrum from the mare is needed to screen for the presence of antibody. Acid-citrate-dextrose (yellow-topped tubes) anticoagulated blood is generally preferred for screening for red blood cell antigens.

†Also offers blood-typing services. Acceptable samples include serum or acid-citrate-dextrose (yellow-topped tubes) anticoagulated blood. Most laboratories offer kits or mailers with appropriate tubes and specific instructions; call for information.

inappetence. These foals are so intent on breathing that they appear reluctant to pause long enough to nurse and consequently are at high risk for secondary complications, including dehydration and septicemia. Foals exhibiting clinical signs of hypotension, weakness, or acidosis or foals with concurrent illness (e.g., septicemia, respiratory disease) generally benefit from blood transfusion.

The severity of the anemia does not always correlate to the need for transfusion; foals that slowly develop more profound anemias over the course of several days appear to compensate more effectively than foals that may develop a less severe anemia more rapidly. Consequently, no exact cut-off exists for the decision to transfuse, and clinical parameters should be considered in addition to the actual RBC number.

Whole blood from a universal donor is the ideal blood product. A suitable donor can be identified by standard blood-typing tests or by cross matching the donor's RBCs with serum or colostrum from the mare. In cases in which an emergency transfusion is needed and testing is not available, blood from a Quarter Horse or Standardbred gelding may have the least potential for reaction with the foal. Aa and Qa are less prevalent in Quarter Horse and Standardbred populations compared with the Thoroughbred population.

Because geldings would not have birth exposure to blood antigens they are an ideal choice; however, a full history should be obtained to determine if the gelding had ever received any equine biologics (blood products, tetanus antitoxin, or equine plasma). The foal's sire is an

unsuitable donor because his RBCs contain the same incriminating antigens as the foal and would be lysed by any remaining maternal antibody. Alternatively, if a compatible donor cannot be identified, washed RBC from the dam can be used for transfusion. However, separating the plasma and washing her RBCs is mandatory before transfusion to ensure removal of circulating anti-RBC antibodies. If anti-RBC antibodies from the dam are transferred to the foal, continued lysis of the foal's remaining RBC will occur and the course of the disease will be extended.

After collection, the dam's RBCs must stand for 1 to 3 hours in the collection bottles; alternatively, if available, a large-volume centrifuge can be used to expedite sedimentation. The plasma is then aseptically aspirated and the RBCs resuspended in an equal volume of sterile 0.9% saline using gentle mixing. This process should be repeated at least one more time before transfusion.

The optimal transfusion volume can be calculated using the formula below, alternatively, 1 to 2 liters of whole blood or washed red blood cells can be given empirically to the foal.

$$\frac{(\text{PCV}_{\text{desired}} - \text{PCV}_{\text{recipient}}) \times \text{Body wt (kg)} \times \text{Blood volume (L/kg)}}{\text{PCV}_{\text{donor}}}$$

where PCV is packed cell volume.

The normal blood volume of a neonatal foal is approximately 0.09 L/kg. Filtered blood transfusion sets should be used to administer blood products to avoid anaphylactic reactions. All transfusions should be started slowly and the foal observed for signs of a transfusion reaction. Signs include elevated respiratory rate, heart rate, agitation, hives, or anaphylactic shock. If no reaction is observed over the first few minutes the rate can be increased and approximately half the volume given rapidly over 30 to 60 minutes. Once the foal has stabilized, the rate should be decreased and the remainder given over the next few hours. Care should be taken when administering blood to avoid circulatory overload in the foal.

The goal of therapy should be resolution of clinical signs associated with decreased oxygen delivery and an overall improvement in the foals attitude and appetite, not simply normalization of its hematocrit. Given the short half-life of transfused cells (2 to 4 days in the adult horse) additional transfusions (up to two or three) may be required to sustain clinical improvement; however, the half-life of transfused RBCs may decrease with subsequent transfusions.

A polymerized hemoglobin product (Oxyglobin, Biopure, Cambridge, Mass.) is available for use when immediate transfusion is necessary and no appropriate donor is available. The time required to prepare red blood cells for transfusion may be excessive in the severely compromised foal. Oxyglobin has been used in NI foals as a "therapeutic bridge" until a blood transfusion can be administered.

Supportive and prophylactic treatments are indicated in addition to treatment of the primary problem, that being decreased oxygen delivery to the tissues. Weak, dehydrated foals have a significant risk for development of complications including sepsis, aspiration pneumonia, and multi-organ failure secondary to hypoxia. Severe bilirubinemia can result in liver damage and kernicterus. Intravascular hemolysis can result in hemoglobin nephropathy and renal failure. In addition to transfusion therapy, broad-spectrum antibiotics are indicated if pneumonia, sepsis, or other infections are suspected. Intranasal oxygen therapy (5 to 8 L/min) may be of some benefit in foals with pneumonia and decreased arterial partial pressure of oxygen in an attempt to improve hemoglobin saturation of the remaining RBCs. Polyionic fluid therapy may be necessary, in addition to a blood transfusion, to replace volume deficits and correct electrolyte and acid base abnormalities. Weak, recumbent foals should be given supplemental nutrition (milk replacer,

beginning at 10% of body weight/day) via nasogastric intubation, or partial/total parental nutrition. Weak or recumbent foals should never be bottle-fed because their suckle reflex may be diminished resulting in milk aspiration and subsequent pneumonia.

Corticosteroid therapy (prednisolone 1 mg/kg IV) may be beneficial in reducing the hemolytic process in acute cases of NI. Anticonvulsive therapeutic agents such as diazepam (0.1 to 0.3 mg/kg IV, every 30 minutes as needed) should be used in foals experiencing seizures resulting from brain hypoxia, kernicterus, or sepsis. Continued seizures should be treated with phenobarbital (loading dose of 8 to 16 mg/kg in 50 ml normal saline IV, slow over 30 minutes, followed by 5 to 10 mg/kg in 50 ml normal saline IV q8h, slow over 30 minutes).

PROGNOSIS

The prognosis for NI varies depending on the severity of the disease, with uncomplicated cases carrying a favorable prognosis. Foals with acute, severe anemia, significant tissue hypoxia and seizures have a more guarded prognosis. Occasionally, foals with NI continue to hemolyze after blood transfusions and can develop severe degenerative hepatopathy secondary to overwhelming bilirubinemia. These foals have an extremely grave prognosis. Cases complicated by septicemia, kernicterus, severe aspiration pneumonia, or multi-organ failure also have a poor prognosis.

Supplemental Readings

- Bailey E, Conboy HS, McCarthy PF: Neonatal isoerythrolysis of foals: an update on testing. *Proceedings of the 33rd Annual Convention of the American Association of Equine Practitioners*, pp 341-353, 1987.
- Becht JL, Page EH, Morter RL et al: Evaluation of a series of testing procedures to predict neonatal isoerythrolysis in the foal. *Cornell Vet* 1983; 73(4):390-402.
- Paradis MR: Neonatal transfusion medicine. *Adv Vet Sci Comp Med* 1991; 36:225-237.
- Perkins GA, Divers TJ: Polymerized hemoglobin therapy in a foal with neonatal isoerythrolysis. *J Vet Emerg Crit Care* 2001; 11(2):141-146.
- Whiting JL, David JB: Neonatal isoerythrolysis. *Comp Cont Educ Pract Vet* 2000; 22(10):968-975.

CHAPTER 12.3

Prematurity

GUY D. LESTER

Perth, Western Australia

Many factors can lead to premature delivery of the equine fetus or result in a foal that is inappropriately developed for its gestational age. Prematurity is usually defined as a foal with a gestational age that is less than 320 days. Unfortunately, this definition is complicated by difficulties in establishing normal gestational length. The reported normal gestational range is broad—between 320 and 365 days for the Thoroughbred breed—with a mean duration of 341 days. Consequently, a foal born at 340 days may be premature if its expected duration *in utero* was 360 days. The gestational period is also influenced by breed, time of the year, and fetal gender. A foal that is described as dysmature has physical or hormonal development that is inappropriate for its gestational length. Foals that are born after prolonged gestational periods may have appropriate bone growth but are often thin and weak. These foals are often called postmature and are believed to have outgrown their placentas.

Well-recognized causes of prematurity or dysmaturity include bacterial or viral placental infection, placental insufficiency (e.g., premature placental separation, twinning), maternal disease or anesthesia, or the mistimed administration of oxytocin. Determination of a reason for premature delivery can be helpful in predicting survival. Bacterial infection of the placenta is associated with improved outcomes in foals that are born prematurely. Fescue toxicosis is a known cause of prolonged gestation and postmaturity.

PHYSICAL CHARACTERISTICS OF PREMATURE FOALS

The characteristics of prematurity include a low birth weight, generalized weakness, a short and silky hair coat, an increased range of joint motion, rear limb flexural laxity, and incomplete skeletal ossification (as assessed radiographically). The rear limb laxity will result in transient sloping of the top line from the horizontal—a German Shepherd-type appearance. Premature foals will often take longer (>60 minutes) than term foals to stand and commonly require assistance to do so. They also are slower to suck from the mare (>120 minutes). The suckle reflex may lack vigor. A prominent or domed forehead is commonly seen in foals that have been exposed to intrauterine growth retardation (e.g., in twins). Premature or dysmature foals may also demonstrate flexural laxity or deformity of the forelimbs and floppy ears.

ENDOCRINE MATURATION

A foal born prematurely to a mare with chronic bacterial placentitis will likely stand a much better chance of survival in the extrauterine environment than a foal that is taken by cesarean section or is induced before maturation. This can occur independently of gestational age. Development of the fetal pituitary-adrenal axis late in gestation is essential to the final maturation of various organ systems, especially the respiratory tract. Fetal exposure to cortisol is restricted during most of gestation. Placental 11- β hydroxylase converts maternal cortisol to the less active form, cortisone, and the fetal adrenal responds poorly to adrenocorticotrophic hormone (ACTH) in terms of cortisol production. Progesterone is preferentially converted to reduced pregnanes rather than to cortisol because key steroidogenic enzymes, such as 17 α -hydroxylase, are either inhibited or produced in inadequate amounts.

Fetal cortisol increases significantly during the final 24 to 48 hours before parturition, presumably associated with increased adrenal 17 α -hydroxylase activity. The cortisol surge induces changes in neutrophil and lymphocyte counts, such that the neutrophil to lymphocyte (N:L) ratio exceeds 2.5:1 at the time of birth.

Triiodothyronine (T3) also increases late in gestation, such that the normal neonate has circulating levels of T3 that are 10 to 20 times greater than those seen in the adult animal. These values begin to decline by 24 hours of postnatal life. Thyroid hormones regulate a number of important physiologic functions, including maintenance of an effective body temperature and skeletal development.

Foals removed from their *in utero* environment before endocrine maturation will have relatively low serum levels of thyroid hormone and cortisol and high blood levels of pregnanes and when challenged with exogenous ACTH, will fail to adequately increase cortisol. These foals will not have undergone the essential maturation of body systems that takes place during the final days of gestation and will likely be poorly prepared for survival in the extrauterine environment. In contrast, maturation is hastened when the fetus is exposed to chronic *in utero* stress, thus resulting in a foal that, despite physical immaturity, will often have adequate pulmonary and hematologic function. The mechanism responsible for hastened maturation is not known but could involve cytokine-induced enzyme induction. This maturation does not occur suddenly, and foals are often born with varying degrees of maturation.

FORMULATING A PROGNOSIS

Providing accurate advice to clients as to short- and long-term prognoses can be difficult. The clinical course of the premature foal is often interrupted by a variety of complications—including dysfunction of the musculoskeletal, respiratory, and gastrointestinal systems. Before committing to a treatment plan, the owner should be given a reasonable estimation of short-term and long-term survival, expected costs, and possible complications. The short-term prognosis is based on a variety of factors, which will be discussed in the following text.

Calculation of Gestational Age and the Degree of Physical Maturity

Foals with a gestational length of less than 280 days rarely survive, irrespective of available resources. Foals without a hair coat or with eyelids sutured closed are not candidates for treatment. All premature foals are at risk for severe angular limb deformities because of the combination of ligamentous laxity and poor ossification of cuboidal bones. The relative risk of musculoskeletal deformity is related to gestational age and does not appear to be accelerated by exposure to *in utero* inflammation.

Reason for Premature Delivery

Important endocrine maturation occurs in the last days of gestation. Consequently, foals whose birth is induced before this stage may experience severe and life-threatening problems after birth. Foals that are born prematurely after acute maternal illness also commonly experience difficulty. Hastened endocrine maturation can occur in response to chronic bacterial placentitis, thus greatly improving the chances of postnatal survival. Noninfectious, noninflammatory placental diseases, such as chronic placental separation or diffuse placental edema, do not appear to hasten maturation; on the contrary, they are usually associated with increased perinatal mortality.

Laboratory Data

Premature foals that have a low total WBC count (<5000 cells/ μ l) and a low to normal fibrinogen (100-300 mg/dl) will likely experience trouble in the neonatal period. These foals will typically have a low N:L ratio and low blood cortisol and will fail to produce an adequate rise in cortisol when challenged with ACTH (0.125 mg ACTH IM) during the first 24 hours after birth. A lack of white blood cell (WBC) count elevation by day two is an additional poor prognostic sign.

Data derived from a large population of premature foals indicates that the N:L ratio is a good predictor of postnatal survival. Foals with large elevations in this ratio ($>10:1$) above normal often do well with minimal support. Although the total white count may be greatly elevated ($>20,000$ cells/ μ l), many of these foals have negative blood cultures. Antimicrobial therapy may not be important in determining survival in this subpopulation but is usually administered in the absence of supporting laboratory data.

Sepsis (see Chapter 12.6: "Neonatal Septicemia") is the

most important differential diagnosis and is often represented hematologically by leucopenia and neutropenia. Evidence of shifting towards immature cell types and neutrophil toxicity should point the clinician towards primary sepsis or prematurity complicated by sepsis. Pneumonia or systemic sepsis is a potential complication of bacterial placentitis in premature and dysmature foals.

Positive outcomes are also associated with elevations in fibrinogen concentration and negatively associated with increased total blood calcium concentrations. Premature foals without sepsis will often return a positive sepsis score as they often share clinical and laboratory features of septic foals—including neutropenia, hypoglycemia, and systemic weakness.

Factors in the Perinatal Period

The premature foal is particularly vulnerable to added stresses during the perinatal period. Perinatal asphyxia is common in these foals because of the common association between placental diseases and prematurity. An episode of moderate to severe asphyxia will severely complicate the clinical course. Likewise, meconium aspiration will add an additional stress on an immature cardiopulmonary system. These foals are at risk for sepsis because of the combination of an immature immune system and a lack of maternal colostrum. They also tend to spend more time in recumbency than term foals, thereby increasing their exposure to environmental pathogens.

Availability of Resources

Hormonally mature foals will often do well with minimal veterinary support. The management of premature or dysmature foals that have not experienced accelerated hormonal maturation or of those with complications usually requires access to appropriate physical and labor resources. In the event of impending respiratory failure, this could necessitate access to veterinarians with facilities and experience in mechanical ventilation (see Chapter 12.5: "Cardiopulmonary Resuscitation of the Newborn Foal"). In addition, the owner must undertake a substantial financial commitment; intensive care of premature or dysmature foals can be expensive.

CLINICAL PROGRESSION

The clinical progression will reflect the degree of endocrinologic maturity, additional perinatal stresses (e.g., asphyxia, sepsis, meconium aspiration), and the level of physical maturity. Typically foals born prematurely, except if they are exposed to chronic *in utero* stress, initially are weak and depressed. Some will require resuscitation after birth (see Chapter 12.5: "Cardiopulmonary Resuscitation of the Newborn Foal"). After a longer-than-normal period of postural adaptation they will usually manage to stand but often need assistance. Suckle reflex and appetite are often reduced or absent, and many will need to be fed colostrum and milk via a nasogastric tube. They will often have trouble maintaining their body temperatures and blood glucose levels. After the initial 24-hour period many of these foals demonstrate improvement both in physical

strength and mentation. Their appetite for milk will often exceed that of a term foal.

The hormonally immature foal will commonly require immediate resuscitation. These foals will often mimic the clinical progression of the hormonally-mature or "stressed" premature foals up until 12 to 18 hours of age, after which time a range of progressive abnormalities may develop. The expectations of owners may be falsely raised as many foals immediately after birth will appear bright and alert, will vocalize, and make frequent but unsuccessful attempts to stand. Progressive abnormalities that develop later include systemic weakness, depression, seizures, respiratory acidosis, and intolerance to enteral feeding and bloat. Cardiovascular collapse—the first sign of which is a reduction in the intensity of peripheral pulses—may ensue and may be followed by oliguria, subcutaneous edema, and further deterioration in neurologic status. Poor tissue perfusion leads to lactate production and a mixed metabolic and respiratory acidosis. Death will occur without aggressive support, and even with high level intensive care mortality rates are high.

BODY TEMPERATURE AND GLUCOSE

Premature foals are more susceptible to hypothermia than term neonates are. These foals are likely deficient in brown adipose tissue and lack the ability to maintain body heat through shivering. Low thyroid hormone levels have also been associated with hypothermia in foals. Body temperature needs careful management; rapid warming may result in peripheral vasodilatation and cardiovascular collapse. Initially, the foal should be covered by blankets and removed from any drafts. Intravenous and oral fluids should be warmed before use. Once the foal begins to demonstrate vigor, heat lamps and circulating warm-water blankets can be used.

The premature foal has inadequate glycogen stores at birth and is at risk for hypoglycemia. This is managed acutely by rapid infusion of 10 ml/kg of a 10% dextrose solution over several minutes and is followed by a constant infusion at about 6 ml/kg/minute of a 5% dextrose-containing fluid (approximately 200 ml/hour of a 5% dextrose solution to a 30-kg foal). Bolus administration of hypertonic glucose-containing solutions should be avoided.

CARDIOPULMONARY SYSTEM

Most premature foals have some degree of respiratory insufficiency. The low arterial oxygen concentration in healthy newborn foals is further accentuated in the dysmature or premature foal. Extrapulmonary shunts can account for more than 30% of cardiac output, in contrast to less than 10% in normal full-term foals. In addition, ventilation/perfusion inequalities may occur as a result of alveolar collapse or atelectasis, the severity of which is influenced by maturation of the surfactant system. Lung surfactant is produced from type II alveolar epithelial cells and is composed of phospholipids (including dipalmitoyl phosphatidylcholine and phosphatidylglycerol), inert lipids, and protein. It prevents spontaneous collapse of the alveoli by reducing alveolar surface tension. Surfactant activity can be detected in the developing fetus by 100 days

but is not fully developed until 300 days or—in some foals—not until after birth. Deficiency of surfactant has been implicated as the major contributing factor to the development of neonatal respiratory distress syndrome (RDS) or hyaline membrane disease in premature animals. This is associated with a severe respiratory acidosis with secondary, hypoxia-induced pulmonary arterial hypertension, reduced cardiac output, and tissue hypoxia. A highly proteinaceous fluid is leaked into the interstitium and alveoli. This results in the radiographic finding of air bronchograms. Fibrinogen in the edema fluid is converted into fibrin, the so-called hyaline membranes observed histologically in neonatal RDS. Dramatically improved survival rates have been achieved in human infants with RDS since the release of bovine or synthetic surfactant. Classic neonatal RDS occurs in premature foals but is relatively uncommon. In contrast, a milder form of the syndrome—characterized clinically by reduced ventilation capacity, tachypnea, hypoxemia, and progressive hypercapnia—is relatively common. Radiographically, interstitial density without air bronchograms diffusely increases. The administration of exogenous surfactant to premature foals at risk for respiratory failure has been beneficial to a small number of animals but is usually prohibitively expensive. Moreover, objective controlled studies are lacking.

Management of the failing cardiovascular system is also challenging. Successful treatment relies upon early detection of falling systemic blood pressure. Close monitoring for signs of peripheral edema or less than anticipated urine output can also signal an impending problem. Maintenance of mean blood pressure (>60 mm Hg) appears to be critical in the prevention of a fatal downward spiral of cardiopulmonary collapse with secondary renal and gastrointestinal failure. An initial approach to treatment commonly involves intravenous plasma followed, if necessary, by dopamine infusion at 3 to 5 µg/kg/min. If this is ineffective, dobutamine (5-20 µg/kg/min) or vasopressin (0.25-0.5 mU/kg/min) infusion can be attempted. Overadministration of sodium-containing fluids can often lead to hyponatremia and widespread edema.

MUSCULOSKELETAL SYSTEM

Skeletal maturity is assessed by radiographic examination of both the carpus and tarsus for evidence of incomplete ossification. Management of the foal with incomplete skeletal ossification is controversial. Most experts believe that exercise should be restricted to minimize collapse of developing carpal or tarsal bones, but forced recumbency may predispose the foal to or exacerbate pulmonary disease. Restricted stall exercise with splinting is commonly recommended. Assessment of joint and tendon laxity is also important. The excessive joint laxity of premature foals predisposes them to acquired angular limb deformities.

IMMUNE SYSTEM

The premature foal is at increased risk for developing secondary bacterial disease over a healthy term neonate. Chronic placental disease is often associated with premature lactation that results in an inadequate quality and quantity of colostrums and predisposes to failure of pas-

sive transfer. The dams of prematurely induced foals or foals taken by cesarean section may have failed to produce colostrum. Susceptible animals probably require plasma transfusion and prophylactic antibiotic therapy.

CORTICOSTEROID THERAPY

Corticosteroids are an important prepartum medication administered to women who are in danger of delivering prematurely. Betamethasone administered systemically will cross the human placenta and hasten lung maturation of the fetus. The equine placenta appears to be relatively impermeable to exogenous corticosteroids. Betamethasone injected intramuscularly into the equine fetus by means of ultrasound guidance will hasten maturation, but the technique itself is associated with premature delivery. Given the apparent synergism between thyroid hormone and cortisol, it has been suggested in humans to combine thyrotropin-releasing hormone (TRH) with betamethasone. The value of corticosteroids in preterm newborn foals is controversial. Hydrocortisone infusion holds theoretic benefit, but efficacy and experimental data in foals are lacking. A single injection of ACTH would be unlikely to have efficacy but may have diagnostic or prognostic value. Multiple doses have been advocated in the management of these hormonally immature foals.

LONG-TERM OUTCOMES

Short-term survival rates of premature and dysmature foals have improved over recent years. The long-term outcome as it relates to the athletic potential of these foals has not been adequately described. Data derived from a small population of surviving commercial Thoroughbred foals suggests that these foals may not be as likely to make it to the racetrack, and those that do are commonly not as successful as their siblings.

Supplemental Readings

- Chavatte P, Holtan D, Ousey JC et al: Biosynthesis and possible biological roles of progestagens during equine pregnancy and in the newborn foal. *Equine Vet J* 1997; 24(Suppl):89-95.
- Chavatte PM, Rossdale PD, Tait AD: Modulation of 3 beta-hydroxysteroid dehydrogenase (3 beta-HSD) activity in the equine placenta by pregnenolone and progesterone metabolites. *Equine Vet J* 1995; 27:342-347.
- Irvine CH, Evans MJ: Postnatal changes in total and free thyroxine and triiodothyronine in foal serum. *J Reprod Fertil* 1975; 23(Suppl):709-715.
- Rossdale PD: Clinical view of disturbances in equine foetal maturation. *Equine Vet J* 1993; 14(Suppl):3-7.
- Silver M, Fowden AL, Knox J et al: Relationship between circulating triiodothyronine and cortisol in the perinatal period in the foal. *J Reprod Fertil* 1991; 44(Suppl):619-626.

CHAPTER 12.4

Perinatal Asphyxia Syndrome in Foals

WENDY E. VAALA
Oldwick, New Jersey

Asphyxia during late pregnancy and/or delivery causes a decrease in tissue perfusion and oxygenation in the newborn foal and results in a spectrum of clinical signs—including neurologic deficits that range from hypotonia to grand mal seizures; gastrointestinal disturbances that range from mild ileus and delayed gastric emptying to severe, bloody diarrhea and necrotizing enterocolitis (NEC); and renal compromise accompanied by varying degrees of oliguria. Based on the neurologic deficits—including loss of affinity for the dam, seizures, abnormal vocalization, and aimless wandering—affected foals have been called “dummies,” “convulsives,” “barkers,” and “wanderers.” Neonatal maladjustment syndrome (NMS) is a common term used to describe this condition. Hypoxic ischemic encephalopathy (HIE) is a more precise medical term to describe the central nervous system (CNS) disturbances, which include edema, necrosis, and occasional hemorrhage.

Asphyxia is the result of impaired oxygen delivery and usually results from a combination of hypoxemia (decreased oxygen concentration in the blood) and ischemia (decreased perfusion). Ischemia is far more devastating and results in anaerobic metabolism, increased blood lactate concentrations, and intracellular acidosis and is a preamble for reperfusion injury. Perinatal brain damage occurs when the fetus can no longer maintain adequate cerebral circulation. Acute and delayed neuronal cell death ensues. Mild asphyxia produces transient tissue ischemia with potentially reversible damage. Prolonged ischemia results in disruption of tight junctions in the capillary endothelium and leakage of osmotic agents and fluid into surrounding brain interstitium, thus resulting in vasogenic edema. Brain necrosis occurs and is accompanied by increased intracranial pressure, progressive brain swelling, reduced cerebral blood flow, and exacerbation of existing ischemia.

sive transfer. The dams of prematurely induced foals or foals taken by cesarean section may have failed to produce colostrum. Susceptible animals probably require plasma transfusion and prophylactic antibiotic therapy.

CORTICOSTEROID THERAPY

Corticosteroids are an important prepartum medication administered to women who are in danger of delivering prematurely. Betamethasone administered systemically will cross the human placenta and hasten lung maturation of the fetus. The equine placenta appears to be relatively impermeable to exogenous corticosteroids. Betamethasone injected intramuscularly into the equine fetus by means of ultrasound guidance will hasten maturation, but the technique itself is associated with premature delivery. Given the apparent synergism between thyroid hormone and cortisol, it has been suggested in humans to combine thyrotropin-releasing hormone (TRH) with betamethasone. The value of corticosteroids in preterm newborn foals is controversial. Hydrocortisone infusion holds theoretic benefit, but efficacy and experimental data in foals are lacking. A single injection of ACTH would be unlikely to have efficacy but may have diagnostic or prognostic value. Multiple doses have been advocated in the management of these hormonally immature foals.

LONG-TERM OUTCOMES

Short-term survival rates of premature and dysmature foals have improved over recent years. The long-term outcome as it relates to the athletic potential of these foals has not been adequately described. Data derived from a small population of surviving commercial Thoroughbred foals suggests that these foals may not be as likely to make it to the racetrack, and those that do are commonly not as successful as their siblings.

Supplemental Readings

- Chavatte P, Holtan D, Ousey JC et al: Biosynthesis and possible biological roles of progestagens during equine pregnancy and in the newborn foal. *Equine Vet J* 1997; 24(Suppl):89-95.
- Chavatte PM, Rossdale PD, Tait AD: Modulation of 3 beta-hydroxysteroid dehydrogenase (3 beta-HSD) activity in the equine placenta by pregnenolone and progesterone metabolites. *Equine Vet J* 1995; 27:342-347.
- Irvine CH, Evans MJ: Postnatal changes in total and free thyroxine and triiodothyronine in foal serum. *J Reprod Fertil* 1975; 23(Suppl):709-715.
- Rossdale PD: Clinical view of disturbances in equine foetal maturation. *Equine Vet J* 1993; 14(Suppl):3-7.
- Silver M, Fowden AL, Knox J et al: Relationship between circulating triiodothyronine and cortisol in the perinatal period in the foal. *J Reprod Fertil* 1991; 44(Suppl):619-626.

CHAPTER 12.4

Perinatal Asphyxia Syndrome in Foals

WENDY E. VAALA
Oldwick, New Jersey

Asphyxia during late pregnancy and/or delivery causes a decrease in tissue perfusion and oxygenation in the newborn foal and results in a spectrum of clinical signs—including neurologic deficits that range from hypotonia to grand mal seizures; gastrointestinal disturbances that range from mild ileus and delayed gastric emptying to severe, bloody diarrhea and necrotizing enterocolitis (NEC); and renal compromise accompanied by varying degrees of oliguria. Based on the neurologic deficits—including loss of affinity for the dam, seizures, abnormal vocalization, and aimless wandering—affected foals have been called “dummies,” “convulsives,” “barkers,” and “wanderers.” Neonatal maladjustment syndrome (NMS) is a common term used to describe this condition. Hypoxic ischemic encephalopathy (HIE) is a more precise medical term to describe the central nervous system (CNS) disturbances, which include edema, necrosis, and occasional hemorrhage.

Asphyxia is the result of impaired oxygen delivery and usually results from a combination of hypoxemia (decreased oxygen concentration in the blood) and ischemia (decreased perfusion). Ischemia is far more devastating and results in anaerobic metabolism, increased blood lactate concentrations, and intracellular acidosis and is a preamble for reperfusion injury. Perinatal brain damage occurs when the fetus can no longer maintain adequate cerebral circulation. Acute and delayed neuronal cell death ensues. Mild asphyxia produces transient tissue ischemia with potentially reversible damage. Prolonged ischemia results in disruption of tight junctions in the capillary endothelium and leakage of osmotic agents and fluid into surrounding brain interstitium, thus resulting in vasogenic edema. Brain necrosis occurs and is accompanied by increased intracranial pressure, progressive brain swelling, reduced cerebral blood flow, and exacerbation of existing ischemia.

An important mediator of ischemic tissue damage is the fast excitatory neurotransmitter glutamate. At high extracellular concentrations, glutamate acts as a neurotoxin and mediates opening of ion channels that permit sodium to enter cells and is followed by an influx of chloride ions and water, thus resulting in osmotic lysis and immediate neuronal death. Glutamate also mediates delayed cell death by provoking calcium influx through depolarization-induced opening of calcium channels and by direct stimulation of N-methyl-D-aspartate (NMDA) receptors that open additional calcium channels. High intracellular levels of free calcium result in activation of enzyme systems, generation of free radicals, and impaired mitochondrial function that results in delayed neuronal death.

Additional brain injury occurs as a result of repeated seizures, which are common during severe encephalopathy. Repeated seizures cause brain injury through (1) hypoventilation and apnea resulting in hypoxemia and hypercapnia, (2) elevation in arterial blood pressure and cerebral blood flow, (3) progressive neuronal injury due to excessive release of excitatory amino acids such as glutamate, and (4) depletion of the brain's limited energy stores to support seizure activity.

In utero, fetal compensatory mechanisms against increasing asphyxia include bradycardia; decreased oxygen consumption; anaerobic glycolysis; and redistribution of blood flow with preferential perfusion of the brain, heart, and adrenal glands at the expense of circulation to kidneys, gut, liver, lungs, and muscle. The extent of tissue injury depends on whether the asphyxial insult is acute or chronic and partial or complete and on whether the neonate is premature or full-term. Chronic hypoxia slows fetal growth in a pattern that reflects asphyxia-induced redistribution of blood flow. Brain and bone are spared; gut, liver, and fat are not. The result is a fetus with a small body and large head. This form of *in utero* growth retardation (IUGR) is termed disproportionate. Chronic *in utero* hypoxia may also produce relative renal ischemia in the fetus with a decrease in urine production. Because fetal urine is a major component of fetal fluids, chronic hypoxia may be associated with a decrease in fetal fluid volumes.

PERIPARTURIENT EVENTS

Periparturient asphyxia (PAS) can result from any event that impairs uteroplacental perfusion prepartum or intrapartum or that disrupts normal distribution of blood flow postpartum. PAS has been associated with normal deliveries, dystocias, induced deliveries, cesarean sections, placentitis, premature placental separation, meconium-stained foals, twinning, severe maternal illness, and post-term pregnancies.

Dystocias produce acute and chronic hypoxia through a variety of mechanisms—including cord compression and thoracic trauma with damage to the heart and lungs. Induction may induce a dystocia or predispose to premature placental separation. Cesarean section jeopardizes uteroplacental perfusion as a result of maternal hypotension that is caused by anesthetic depression and placement of the dam in dorsal recumbency. Placentitis can cause acute and chronic placental insufficiency and hypoxia as well as neonatal septicemia. Placental separation

causes varying degrees of asphyxia depending whether the separation is acute or chronic, complete or partial. Meconium staining of the foal and fetal fluids or placenta is associated with fetal distress and hypoxia. Hypoxia results in intestinal ischemia, hyperperistalsis, anal sphincter relaxation, and *in utero* passage of meconium. Fetal meconium aspiration may further compromise neonatal respiration by inducing pulmonary hypertension, chemical pneumonitis, airway obstruction, regional lung atelectasis, and surfactant dysfunction. Twinning can be associated with placental insufficiency and prolonged delivery.

Mares with reproductive tract disease such as placentitis (see Chapter 5.24: "Placentitis"), hydrops allantois (see Chapter 5.25: "Placental Hydrops"), hydrops amnii, or prepubic tendon rupture (see Chapter 5.27: "Ventral Abdominal Hernia and Prepubic Tendon Rupture") are more likely to deliver hypoxic foals. Severe maternal illness accompanied by anemia, hypoproteinemia, or endotoxemia can alter uteroplacental blood flow. Postterm pregnancies have been associated with varying degrees of placental insufficiency and the birth of small, underweight, maladapted foals. Postpartum severe neonatal cardiopulmonary disease can contribute to hypoxic, ischemic tissue damage.

CLINICAL SIGNS

During severe *in utero* hypoxia a sequential loss of fetal reflexes occurs; the most oxygen-demanding fetal activities disappear first. Fetal reflexes are lost in the following order: (1) fetal heart rate reactivity (the ability to increase heart rate in response to fetal activity), (2) fetal breathing, (3) generalized fetal movements, and (4) fetal muscle tone. These biophysical events—in addition to amniotic and allantoic fluid volume estimation and placental integrity—can be evaluated in the late pregnant mare through transabdominal ultrasonography. Signs that suggest fetal or placental compromise during the last month of gestation include persistent fetal bradycardia (fetal heart rate [FHR] <50-60 bpm), loss of FHR variability, reduced or absent fetal movement, decreased volume of fetal fluids (maximum ventral fetal fluid pocket depths average 8 cm for amniotic fluid and 13 cm for allantoic fluid), large areas of placental separation, and generalized placental thickening (combined uteroplacental thickness >12-15 mm).

Signs of peripartum asphyxia in the newborn foal become apparent during the first 24 to 72 hours of life. Severely affected foals show signs immediately postpartum. HIE is associated with a host of behavioral abnormalities—including loss of coordinated swallowing and sucking reflexes, inability to locate the udder, tendency to wander away from the mare and walk into walls, generalized hypotonia, and seizures.

Mild hypoxia causes jitteriness and hyperexcitability and may go unrecognized. Moderate hypoxia results in stupor, somnolence, lethargy, and hypotonia that may be accompanied by epileptiform seizures and episodes of extensor rigidity and opisthotonos during recumbency. Moderate hypoxia is also associated with loss of suckle, dysphagia, decreased tongue tone, odontopris, central blindness, mydriasis, anisocoria, nystagmus, and head tilt. Limb deficits and generalized spasticity are less common.

Premature foals that are exposed to moderate hypoxia are more likely to experience “subtle seizures” characterized by paroxysmal events—including eye blinking; eye deviation; nystagmus; pedaling movements; a variety of oral-buccal-lingual movements such as intermittent tongue protrusion, sucking behavior, purposeless thrashing; and other vasomotor changes such as apnea, abnormal breathing patterns, and changes in heart rate. Tonic posturing is another subtle seizure activity characterized by symmetric limb hyperextension or flexion and is often accompanied by abnormal eye movements and apnea.

Severe hypoxia results in marked central nervous system depression, coma, and loss of central regulation of respiration, blood pressure, and temperature that leads to death.

Other organ systems in addition to the CNS are affected. Hypoxia results in reduced mesenteric and splanchnic blood flow and varying degrees of renal and intestinal ischemia. Signs of renal compromise include decreased urine production with peripheral edema formation.

Mild hypoxia may cause transient ileus, constipation, and mild colic. The most severe form of intestinal dysfunction is necrotizing enterocolitis (NEC). Splanchnic hypoperfusion compromises intestinal mucosal cell metabolism resulting in diminished production of the protective mucus layer, which allows proteolytic enzymes to begin autodigestion of the mucosal barrier. Bacteria within the gut lumen begin to colonize, multiply, and invade the bowel wall. Intramural gas is produced by certain species of bacteria and pneumatosis intestinalis develops. Possible complications include intestinal rupture, pneumoperitoneum, severe bacterial peritonitis, and septicemia. Clinical signs associated with varying degrees of hypoxic, ischemic gut injury include ileus, gastric reflux, colic, lethargy, abdominal distention, and diarrhea. Reflux and feces may be positive for blood. Generalized sepsis often accompanies NEC. The radiographic hallmark of NEC is *pneumatosis intestinalis* characterized by linear or cystic submucosal gas accumulation within the bowel wall. In foals, transabdominal ultrasonography has been used to identify focal bowel wall thickening and intramural gas accumulation that appears as sharp white echoes.

Adverse effects of asphyxia on cardiopulmonary function include reduced myocardial contractility, left ventricular dysfunction, tricuspid valve insufficiency, cardiac failure, increased pulmonary vascular resistance, pulmonary hypertension, increased atrial pressure, and persistent right-to-left flow of blood across fetal pathways (e.g., patent ductus arteriosus, foramen ovale). Persistent fetal circulation (PFC) patterns exacerbate hypoxemia. During asphyxia-induced pulmonary vasoconstriction, substrate delivery to the pneumocytes is impaired and surfactant production decreases, leading to secondary pulmonary atelectasis. Asphyxia may also affect the breathing center, thereby directly resulting in abnormal breathing patterns, including prolonged apnea. As a result of cardiac insufficiency the foal may develop systemic hypotension, further impairment of renal blood flow, and decreased pulmonary perfusion. Foals with cardiopulmonary dysfunction may show signs of respiratory distress with tachypnea and dyspnea, tachycardia, hypotension, and murmurs.

Hypoxia may impair liver function, which results in icterus and renders the neonate more susceptible to alterations in glucose homeostasis and can result in decreased hepatic defense mechanisms and increased susceptibility to sepsis. Endocrine organ damage associated with hypoxia includes adrenal gland hemorrhage and necrosis. Parathyroid damage and pancreatic injury can contribute to endocrine abnormalities.

LABORATORY FINDINGS

No hematologic or biochemical changes are pathognomonic for peripartum asphyxia. Table 12.4-1 lists clinical signs associated with specific organ system dysfunction and the laboratory abnormalities to anticipate. Severe asphyxia results in metabolic acidosis: pH less than 7.3 and HCO_3^- less than 20 mEq/L. Prepartum placental insufficiency may be associated with neonatal azotemia (creatinine >3.5 mg/dl) and presuckle hypoglycemia (glucose <25–35 mg/dl). Foals that experience hypoxia-induced respiratory depression may develop hypoxemia and respiratory acidosis (PaO_2 <60 mm Hg, PaCO_2 >65–70 mm Hg). If pulmonary hypertension develops, thoracic radiographs show diminished vascular markings because of pulmonary hypoperfusion. Surfactant dysfunction produces diffuse lung atelectasis and a diffuse reticulogranular parenchymal pattern with air bronchograms.

Foals that suffer from necrotizing enterocolitis will have generalized ileus and thickening of the bowel wall with or without intramural gas accumulation visible on transabdominal ultrasonography that uses a 5- to 7.5-MHz transducer.

DIFFERENTIAL DIAGNOSES FOR CENTRAL NERVOUS SYSTEM DISEASE IN FOALS

Not all neurologic abnormalities in newborn foals are due to PAS. Other causes of neonatal neurologic disease include: (1) metabolic disorders (hypocalcemia, hypomagnesemia, hyponatremia, hypernatremia, hyperosmolality [e.g., hyperlipemia, hyperglycemia], severe azotemia, hepatoencephalopathy), (2) infectious conditions (septic meningitis, septicemia/endotoxemia, equine herpesvirus [EHV] 1 infection), (3) CNS malformations (hydrocephalus, agenesis of the corpus callosum, vertebral and spinal cord malformations, cerebellar abiotrophy, occipitoatlantoaxial malformation), (4) cranial or vertebral trauma, and (5) toxins. If severe metabolic derangements, infections, and congenital defects are ruled out, then asphyxia is the most likely cause of the foal's neurologic deficits. Normal serum chemistry values help rule out metabolic disturbances. A normal leukogram—or the absence of severe leukopenia, neutropenia, and toxic neutrophil changes—helps rule out septic conditions. Cerebrospinal fluid analysis is indicated if septic meningitis is a possible differential. Septic meningitis produces an increased nucleated cell count, protein concentration, and immunoglobulin G (IgG) index in the cerebrospinal fluid (CSF). Hypoxic brain damage may result in an increased albumin quotient in the CSF compatible with increased blood-brain barrier permeability.

Table 12.4-1
Clinicopathologic Conditions Associated with Periparturient Asphyxia

Organ System	Clinical Signs	Laboratory Findings	Pathologic Lesions
CNS	Hypotonia, hypertonia, seizures, coma, loss of suckle, proprioceptive deficits, apnea	Increased ICP, increased BBB permeability and albumin quotient	CNS hemorrhage, edema, ischemic necrosis
Renal	Oliguria, anuria, generalized edema	Azotemia, hyponatremia, hypochloremia, abnormal urinalysis	Tubular necrosis
Gastrointestinal	Colic, ileus, abdominal distention, bloody diarrhea, gastric reflux	Occult blood (+) feces and reflux, <i>pneumosis intestinalis</i>	Ischemic mucosal necrosis, enterocolitis, ulceration
Respiratory	Respiratory distress, tachypnea, dyspnea, rib retractions	Hypoxemia, hypercapnia, respiratory acidosis	Hyaline membrane disease, atelectasis, meconium aspiration, pulmonary hypertension
Cardiac	Arrhythmia, weak pulses, tachycardia, edema, hypotension	Hypoxemia, elevated myocardial enzymes	Myocardial infarcts, valvular insufficiency, PFC
Hepatic	Icterus, abnormal mentation	Hyperbilirubinemia, elevated liver enzymes	Hepatocellular necrosis, biliary stasis
Endocrine: adrenals, parathyroids	Weakness, apnea, seizures	Hypocortisolemia, hypocalcemia	Necrosis, hemorrhage

ICP, Intracranial pressure; BBB, blood-brain barrier; CNS, central nervous system; PFC, persistent fetal circulation.

TREATMENT

Information on specific doses of medications for use in the foal can be found in Table 12.4-2. (Additional information is available in Chapter 1.1: "Neonatal Pharmacology and Therapeutics.") Anticonvulsive therapy is crucial to control seizures to prevent recurrent episodes of CNS ischemia and hypoxia and to reduce the risk of neonatal self-trauma. Diazepam is used initially to stop seizures quickly because of its rapid onset of action. Repetitive doses should be avoided to reduce the risk of respiratory depression. Because of its short duration, diazepam should be followed by phenobarbital to control severe or recurrent seizures. Phenobarbital should be given slowly IV to minimize respiratory depression. Foals that receive phenobarbital should have their body temperatures, blood pressures, and respiratory rates monitored. If diazepam and phenobarbital are not available, pentobarbital can be used. Naloxone (0.01-0.02 mg/kg IV) has been used as an opiate antagonist to diminish CNS depression. Thiamine (10-20 mg/kg q12h) can be added to the IV fluids to help preserve aerobic brain metabolism. Thiamine deficiency has been associated with intracellular and extracellular edema and neuronal cell death due to glutamate-induced and NMDA receptor-mediated excitotoxicity. Xylazine should be avoided because it can cause transient hypertension with exacerbation of CNS hemorrhage. Acepromazine also should be avoided because it lowers the seizure threshold.

Cerebral edema occurs in some HIE foals. Intravenous dimethyl sulfoxide (DMSO) is administered as a 20% solution to help reduce brain swelling and intracranial pres-

sure as well as to decrease inflammation and platelet aggregation. DMSO has mild antibacterial and antifungal properties and is a free radical scavenger. An alternative route of DMSO administration is via nasogastric intubation. DMSO should be used cautiously in hypotensive neonates. The osmotic diuretic, mannitol, has been used to treat cerebral edema and to scavenge free radicals. To avoid exacerbation of cerebral edema, intravenous fluid administration should be conservative and fluid balance monitored in anuric or oliguric patients. Low doses of magnesium sulfate administered as a continuous infusion have been used to reduce the hypoxia-induced increase in oxygen free-radical generation. Other medications used for their antioxidant properties include ascorbic acid (vitamin C) and α -tocopherol (vitamin E).

Controversy surrounds the benefits of glucose administration to neonates during the early post-hypoxic period. Possible benefits include a reduced incidence of CNS infarction, attenuated brain damage, and some degree of neuroprotection by stimulating insulin release and by reducing glycolysis, free radical formation, and glutamate-mediated injury. However, hyperglycemia can augment hypoxic brain injury. Therefore avoiding extremes in glucose concentration is best.

Foals that are having seizures should be protected from self-trauma. Techniques to minimize injury include the application of leg wraps and soft head helmets and the use of padded stalls and fleece-covered beds. Application of artificial tears to the eyes helps prevent secondary corneal ulceration.

Fluid therapy should be monitored closely to avoid

Table 12.4-2
Drugs Used to Treat Foals with Periparturient Asphyxia

Organ System	Clinical Sign	Drug Therapy
CNS	Seizures	<i>diazepam</i> : 0.11-0.44 mg/kg IV; inactivated by sunlight and plastic <i>phenobarbital</i> : 2-10 mg/kg IV q12h; give slowly, monitor serum levels <i>pentobarbital</i> : 2-10 mg/kg IV to effect
	CNS edema	<i>DMSO</i> : 0.5-1.0 gm/kg IV as 20% solution over 1 hr; can repeat q12h <i>mannitol</i> : 0.25-1.0 gm/kg IV as 20% solution over 15-20 min; q6-24h <i>magnesium sulfate</i> : 50 mg/kg/hr diluted to 1% and given slowly as a constant infusion over 1 hr; then decreased to 25 mg/kg/hr as a constant rate infusion for up to 24 hr <i>ascorbic acid (vitamin C)</i> : 50-100 mg/kg/day <i>α-tocopherol (vitamin E)</i> : dose not established; this author has used 500 units orally per day
Renal	Oliguria, anuria	<i>dopamine infusion</i> : 2-10 μg/kg/min; monitor blood pressure and pulse <i>furosemide infusion</i> : 0.25-2.0 μg/kg/hr or 0.25-0.5 mg/kg IV q1-6h; monitor serum electrolytes and hydration status <i>mannitol</i> : 0.5-1.0 gm/kg IV as 20% solution over 15-20 min <i>dobutamine infusion</i> : 2-15 μg/kg/min; use if cardiac dysfunction is contributing to hypotension and poor renal perfusion
Gastrointestinal	Ileus, GI distention	<i>erythromycin</i> : 1-2 mg/kg PO q6h; 1-2 mg/kg/hr as IV infusion q6h <i>cisapride</i> : 10 mg PO q6-8h <i>metoclopramide</i> : 0.25-0.5 mg/kg/hr infusion q6-8h <i>bethanechol</i> : 0.03 mg/kg SQ q8h or 0.16-0.2 mg/kg PO q8h
	Ulcers	<i>sucralfate</i> : 20-40 mg/kg PO q6h <i>ranitidine</i> : 5-10 mg/kg PO q6-8h, 1-2 mg/kg IV q8h <i>cimetidine</i> : 15 mg/kg PO q6h; 6.6 mg/kg IV q6h <i>omeprazole</i> : 4.0 mg/kg PO q24h
Cardiac	Hypotension	<i>dopamine infusion</i> : 2-10 μg/kg/min <i>dobutamine infusion</i> : 2-15 μg/kg/min <i>digoxin</i> : 0.02-0.035 mg/kg PO q24h if cardiac failure is suspected
Respiratory	Hypoxemia Apnea	<i>intranasal, humidified oxygen</i> : 2-10 LPM <i>caffeine</i> : loading dose: 10 mg/kg PO; maintenance dose: 2.5-3.0 mg/kg PO q24h
Endocrine system Immune system	Hypocortisolemia FPT, leukopenia	<i>ACTH (depot)</i> : 0.26 mg IM q8-12h <i>hyperimmune plasma</i> : 10-20 ml/kg IV; monitor serum IgG and WBC <i>colostrum</i> : 40 mg/kg IgG orally by bottle or nasogastric tube if foal is <18 hr of age and has a functional gut <i>broad-spectrum bactericidal antibiotics</i> : amikacin (20-28 mg/kg IV q24h) and potassium penicillin (22,000 U/kg IV q6h); ceftiofur (5 mg/kg IV q8-12h)

CNS, Central nervous system; IV, intravenous; q12h, every 12 hours; DMSO, dimethyl sulfoxide; q6-12h, every 6 to 12 hours; PO, by mouth; SQ, subcutaneously; ACTH, adrenocorticotropic hormone; FPT, failure of passive transfer; LPM, liters per minute.

overhydration and hyperosmolar and hypoosmolar states. Low levels of dopamine stimulate dopaminergic receptors and improve renal blood flow and urine production. Moderate doses stimulate beta-1 receptors to increase heart rate and strength of contraction, which help improve renal perfusion by correcting mild cases of hypotension. High doses of dopamine compromise renal and gastrointestinal perfusion and should be avoided. Furosemide works synergistically with dopamine to promote diuresis. Serum electrolytes should be monitored during diuretic therapy.

Ileus that is associated with hypoxic gut damage can result in bowel distention and colic. Nasogastric decom-

pression relieves proximal gut distention. Enema administration stimulates distal colonic function and encourages passage of gas. Metoclopramide, bethanechol, and erythromycin may improve gastric emptying and upper GI function. Cisapride and erythromycin have been used to stimulate small and large intestinal motility. Adequate time for healing of damaged bowel before using prokinetics in a compromised foal is essential. Sonographic examination of the abdomen helps rule out the presence of intussusceptions and other obstructive lesions prior to administering motility modifiers. Severe large bowel distention may require percutaneous trocarization.

To reduce the risk of NEC, asphyxiated foals should have enteral feeding withheld until intestinal motility has returned. Reassuring signs include manure passage, normal borborygmi, and stable vital signs (temperature, blood pressure). Enteral feeding should be started cautiously with fresh mare's milk or colostrum. Foals with severe gastrointestinal dysfunction should have enteral feeds withheld and should be started on parenteral nutrition. Because intestinal ischemia may predispose to ulceration, H_2 blockers (cimetidine, ranitidine), proton pump inhibitors (omeprazole), or cytoprotective agents (sucralfate) are recommended.

Mild to moderate hypoxemia can be treated by increasing the amount of time the foal spends in sternal recumbency or standing and by administering modest flows of humidified intranasal oxygen (2-8 L/min). Foals that suffer severe hypoxemia and hypercapnia ($P_{aO_2} < 40$ mm Hg, $P_{aCO_2} > 65$ mm Hg) require positive pressure ventilation. Respiratory stimulants are used to treat periodic apnea and abnormally slow breathing patterns associated with central depression of the respiratory center. Caffeine is used most commonly to stimulate the respiratory neuronal activity and increase receptor responsiveness to elevated carbon dioxide concentrations. Overdose with respiratory stimulants leads to excessive CNS and to myocardial and gastrointestinal stimulation that results in agitation, seizures, tachycardia, hypertension, colic, and diarrhea. Caffeine is the safest of the methylxanthines.

Maladjusted foals are at increased risk for failure of passive transfer (FPT) due to their abnormal nursing behavior. Serum IgG levels should be evaluated to ensure adequate passive transfer of colostral antibodies. The foal's serum [IgG] should be greater than 800 mg/dl by 18 to 24 hours of age. If [IgG] is less than 800 mg/dl, colostrum and/or plasma is administered to treat hypogammaglobulinemia.

Adequate nutrition must be provided until the foal is able to nurse normally from the mare. A foal should receive at least 10% of its body weight in milk per day administered as small meals every 1 to 2 hours. For example, a 50-kg foal would require a minimum of 5 L, or 11 pints of milk, per day divided into 10 to 12 feedings per day. If the foal has a strong suckle reflex and coordinated swallow, milk can be offered by bottle. If the suckle or

swallow reflexes are ineffective, then milk should be administered via a nasogastric tube. Parenteral nutrition is required if the foal is experiencing severe necrotizing enterocolitis. Until the foal is able to nurse, the mare should be hand-milked every 2 to 3 hours.

Expecting stabilization of CNS signs within the first 48 to 72 hours after delivery and then followed by gradual improvement in neurologic signs within the first 3 to 5 days is reasonable. Some foals may not regain the ability to nurse from the mare for 7 to 10 days or longer.

PROGNOSIS

With proper support, 70% to 80% of foals suffering from HIE and perinatal asphyxia recover. Most foals recover completely. Foals with the poorest prognosis develop sepsis; fail to show any signs of neurologic improvement within the first 5 days of life; remain comatose and difficult to arouse; and/or experience severe, recurrent seizures. Dysmature and premature foals suffering from prolonged *in utero* hypoxia are more likely to experience refractory hypotension and persistent subtle seizure activity than term foals. Poor prognostic signs include refractory hypotension and oliguria, signs of severe brainstem damage—including loss of thermoregulatory control and profound apnea—and seizures that persist past 5 days of age despite anticonvulsant therapy. Rare, long-term CNS sequelae include unusual docility as adults, vision impairment, residual gait spasticity, and recurrent seizures. Many of the "survivors" have gone on to perform successfully as racehorses and other athletes.

Supplemental Readings

- Vaala WE: Peripartum asphyxia. *Vet Clin North Am Equine Pract* 1994; 10(1):187-218.
- Vaala WE, House JK: Perinatal adaptation, asphyxia, resuscitation. In Smith BC (ed): *Large Animal Internal Medicine*, 3rd edition, pp 266-276, Philadelphia, Mosby, 2002.
- Wilkins PA: Magnesium infusion in hypoxic ischemic encephalopathy. *Proceedings of the American College of Veterinary Internal Medicine Forum*, pp 242-244, 2001.

CHAPTER 12.5

Cardiopulmonary Resuscitation of the Newborn Foal

KEVIN T.T. CORLEY

North Mymms, United Kingdom

MARTIN O. FURR

Leesburg, Virginia

Newborn foals, without any underlying disease, can suffer cardiopulmonary arrest as a result of the birthing process. This makes them better candidates for resuscitation than horses that undergo arrest as a result of a disease process. Veterinarians need to acquire an understanding of cardiopulmonary resuscitation (CPR), in advance of these skills being required. When a foal has a cardiopulmonary arrest, the situation is often tense and it is the role of the veterinarian to calmly direct other people, who may have no or only rudimentary knowledge of CPR. Sometimes this direction is by telephone because veterinarians are often absent at the time of foaling. Arranging training sessions for staff of larger breeding farms before the foal season is another way in which veterinarians can direct CPR.

Time is clearly the most important factor in CPR. This means that early recognition of the foal undergoing arrest, readily available equipment, and an ordered plan are essential for a successful outcome.

FOALS THAT REQUIRE RESUSCITATION

Normal stage two labor should take less than 20 minutes. The normal foal takes a few gasps initially but should be breathing regularly within 30 seconds of birth. The heart rate averages 70 beats per minute (bpm) immediately after birth and should be regular. A few normal foals may have arrhythmias for up to 15 minutes after birth, including atrial fibrillation, wandering pacemaker, atrial premature contraction, and ventricular premature contractions. These dysrhythmias do not require specific treatment. Foals have pain and sensory awareness at birth and develop a righting reflex with 5 minutes and a suck reflex within 2 to 20 minutes.

During cardiopulmonary arrest, either the cardiovascular system or the respiratory system fails first. The other system then fails because its oxygen demands can no longer be met. Respiratory arrest is always primary in the newborn foal. The arrest is usually a result of asphyxia, itself caused by premature placental separation, early severance or twisting of the umbilical cord, prolonged dystocia, or airway obstruction by fetal membranes. Some foals are apneic without any apparent birthing misadventure.

Foals that are deprived of oxygen undergo a sequence of

changes that begin with a brief period of rapid breathing. As the asphyxia continues, the heart rate decreases, respiratory movements cease, and the foal enters primary apnea. During primary apnea, spontaneous breathing can, in some cases, be induced by tactile stimulation. The next stage is irregular gasps, which become weaker until the foal enters secondary apnea. No further respiratory efforts take place and the heart rate continues to decrease until it stops. Part or all of this sequence may occur *in utero* or during delivery; consequently, a foal may already be in secondary apnea by the time it is born. Primary apnea cannot be distinguished from secondary apnea based on clinical signs.

Foals that gasp for longer than 30 seconds have a heart rate consistently below 60 bpm or have obvious dyspnea, and foals with absent respiratory movements or heartbeat require resuscitation (Figure 12.5-1). Foals at risk of undergoing arrest should be identified before foaling so that a veterinarian may be present. Risk factors include vaginal discharge during pregnancy, placental thickening (identified by ultrasonography), any illness of the dam during pregnancy, and delivery by cesarean section.

EQUIPMENT FOR CARDIOPULMONARY RESUSCITATION

Although foals occasionally can be successfully resuscitated with little or no equipment (by mouth-to-nose resuscitation), a small amount of equipment can greatly improve the chances of success. The basic list of equipment is clean towels, 8-mm and 10-mm internal diameter 55-cm-long nasotracheal tubes (V-PFN-8 and V-PFN-10, Cook Veterinary Products, Bloomington, Ind.), a 5-ml syringe to inflate the cuff of the nasotracheal tube, a self-inflating resuscitation bag, a bulb syringe, a small flashlight (pen torch), a bottle of epinephrine (adrenaline, epinephrine injection 1:1000 [Butler, Dublin, Ohio]), five 2-ml sterile syringes and 20-gauge 1-inch and steel 14-gauge 1- to 1½-inch needles. Disposable resuscitation bags (Laerdal "The Bag" Disposable Resuscitator Adult 840043, Wappingers Falls, N.Y.), which can be reused after thorough cleaning, are considerably less expensive to purchase than reusable bags.

Additional equipment includes an oxygen cylinder and flow meter, three 1-liter bags of lactated Ringer's solution, fluid administration set, 14-gauge intravenous catheter, a

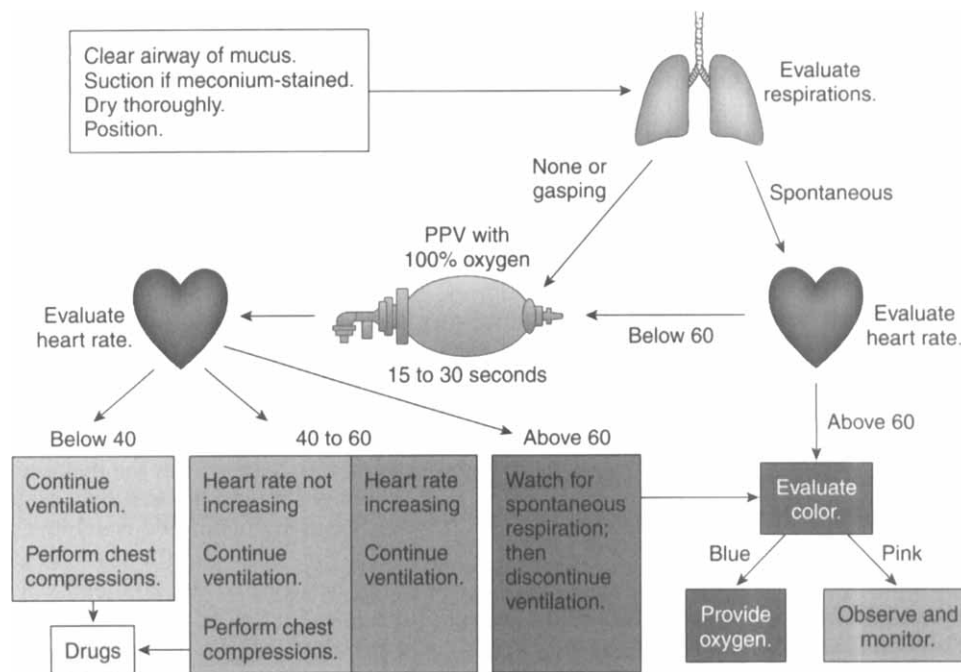


Figure 12.5-1 A flowchart illustrating decision making in resuscitation of the newborn foal. PPV, Positive pressure ventilation.

6 French dog urinary catheter, 2% injectable lidocaine (lignocaine) solution, bretylium tosylate, and an electrical defibrillator. Breeding farms without resident veterinarians should consider purchase of a suitable facemask together with a resuscitation bag or pump (C.D. Foal Resuscitator, McCulloch Medical Products, Glenfield, New Zealand). The equipment for CPR should be placed in a dedicated, single, easily carried container. All CPR equipment should be checked thoroughly before the foaling season.

ORDERED PLAN FOR CARDIOPULMONARY RESUSCITATION

The most critical element in successful CPR is an ordered plan. The basic elements of the plan are airway, breathing, circulation, and drugs (in that order).

First 20 Seconds: Preparing for Cardiopulmonary Resuscitation

In a newborn foal, the first 20 seconds are devoted to assessing the foal and preparing for CPR (see Figure 12.5-1). The extent of action at this point depends on the clinical likelihood that the foal will require resuscitation. In the foal born by cesarian section, these 20 seconds are spent vigorously drying the foal with clean towels, manually clearing the mouth of secretions, and positioning the foal in lateral recumbency on a firm, dry surface. Vigorous drying provides tactile stimulation, which in some cases may be sufficient to start spontaneous breathing. In a foal born with meconium staining, these 20 seconds should be devoted to suctioning the airway. Ideally, airway suctioning should begin as soon as a meconium-stained head appears at the vulva, before the foal takes its first breath. Clearly, early suctioning is not always possible. If the foal is cov-

ered in thick meconium, suctioning of the trachea also should be attempted. Suctioning of the oropharynx can induce bradycardia or even cardiac arrest via vagal reflexes; suctioning with a bulb syringe may be safer than using a mechanical unit. Mechanical suction should not be applied for longer than 5 to 10 seconds at a time. An aspiration mask for clearing the airways is included as part of a commercially available pump and mask system and may be appropriate especially for suction by nonveterinarians. In a foal born normally within 20 minutes, these 20 seconds consist of quiet observation to ensure that the foal's airway is clear and it is spontaneously breathing.

Airway

The best way to ensure an adequate airway is to intubate the foal. Intubation via the nose is preferred to intubation via the mouth because less risk exists of the tube becoming damaged as the foal regains consciousness. If the first two attempts at nasotracheal intubation are unsuccessful, these authors recommend that further attempts should be via the mouth. Ideally, intubation should be completed within less than 30 seconds.

For intubation, the foal can be in lateral or sternal recumbency. The head should be extended so that it is in a straight line with the neck. To pass a tube via the nose, the tube should be held so that it curves downward. One hand should be used to push the tip of the tube medially and ventrally in the nares, into the ventral meatus. The other hand is used to advance the tube smoothly. When the tube reaches the nasopharynx, gentle rotation in either direction can help it slip through the larynx and into the trachea. To pass a tube via the mouth, the tongue should be pulled gently forward and to the side with one hand. This helps to stabilize the larynx. Again the tube is held so that it curves

downward and is advanced smoothly over the tongue, in a midline position. Rotation of the tube when the end is in the oropharynx also can be helpful. Once the tube is in place, the cuff of the tracheal tube should be inflated gently.

The veterinary practitioner must check that the tube has passed successfully into the trachea and did not enter the esophagus, by compressing the thorax and simultaneously feeling the expired air at the proximal tube end. The thoracic wall also should be seen to rise when the first breath is given. If the tube has entered the esophagus, it often can be felt in the cranial neck just left and dorsal to the larynx or proximal trachea. Sometimes, applying pressure to this area of the esophagus by applying gentle pressure either side of the neck can help prevent the tube entering the esophagus.

Breathing

The optimum rate of ventilation is not known in the foal, but experience suggests rates between 10 and 20 breaths per minute are appropriate. If available, 100% oxygen should be used for resuscitation. However, studies of human neonate CPR suggest that resuscitation with room air is equally as effective, and resuscitation certainly should not be delayed if oxygen is not immediately available. The best method of providing artificial respiration is a self-inflating resuscitation bag connected to a nasotracheal or endotracheal tube. This allows controlled ventilation and avoids the risk of aerophagia, or forcing material (such as meconium or mucus) into the airways. Aerophagia can constrain ventilation significantly, because filling the stomach with gas can put pressure on the diaphragm and prevent the lungs from fully expanding.

When a self-inflating resuscitation bag is used, it is physically tiring to squeeze the bag between thumbs and fingers or between hands. The best method is to place the bag against the firm surface (usually the floor) and to kneel next to the bag with the shoulders over the bag. The hands should be placed flat and together, on the bag. This allows a gentle rocking motion and controlled use of body weight to help compression of the bag. Many commercially available self-inflating resuscitation bags have a pressure release valve, to limit the pressure to 30 to 40 cm H₂O. This is the maximum pressure that should be applied for the first breath. Subsequent breaths should require a pressure of only 15 to 20 cm H₂O. The design of some resuscitation bags includes a positive end-expiratory pressure (PEEP) valve. The use of PEEP during CPR increases blood oxygenation but decreases carotid artery blood flow. It is currently unclear whether the use of PEEP is beneficial, harmful, or equivocal.

An alternative to a self-inflating resuscitation bag is a resuscitation pump. It has been recognized recently that excessive volume (*volutrauma*, resulting in emphysema) is more damaging to lungs than excessive pressure (*barotrauma*), and pumps prevent delivery of excess volume. The commercially available model delivers a tidal volume of 780 ml and can be connected to oxygen. It can be connected to a nasotracheal tube or to a mask. Anesthetic machines with a minimum reserve bag of 1 liter and oxygen demand valves also may be used for resuscitation but carry a significant risk of trauma to the lung by use of too large a tidal volume.

Any of the previously discussed delivery devices can be connected to a tight-fitting facemask, rather than a nasotracheal tube. A mask probably represents the best option for CPR not administered by a veterinarian or experienced veterinary technician. The disadvantages of a mask are that it may cause aerophagia, may force mucus or other material into the airways, and can leak. Aerophagia can be reduced by gentle occlusion of the esophagus over the larynx. However, this may require an extra person.

As mentioned previously, foals occasionally can be resuscitated successfully with no equipment, by mouth-to-nose resuscitation. With the foal in lateral recumbency, one hand should be used to cup the chin and occlude the down nostril. The other hand should support the back of the head. The head should be dorsiflexed as far as possible to straighten the airway, but the head should not be lifted. The esophagus should be occluded, as described above, if possible. Resuscitators should watch to check that the thorax rises as they blow into the foal's nostril. Again, the rate should be between 10 and 20 breaths per minute.

Doxapram historically was recommended for stimulating respiration at birth. The drug has been shown to reduce cerebral blood flow and to increase myocardial oxygen demands in experimental animals. Doxapram is therefore no longer recommended.

Circulation

Most human infants who require artificial ventilation at birth do not need chest compressions, and the same is probably true of foals. At 30 seconds after starting ventilation, the foal should be assessed to decide whether circulatory support is required. Thoracic compressions should be started if the heartbeat is absent, less than 40 beats per minute, or less than 60 beats per minute and not increasing (see Figure 12.5-1).

The optimum rate for thoracic compressions in the foal is not known. A rate of 80 compressions per minute (cpm) has been shown to result in significantly better circulation than 40 or 60 cpm in adult horses. Rates between 80 and 120 cpm are therefore likely to be appropriate for foals. However, rates this high rapidly fatigue the resuscitator. Therefore if sufficient people are available, the person doing thoracic compressions should be replaced every 2 to 5 minutes. Continuation of ventilation during thoracic compressions is vital. The recommended ratio is two breaths per 15 thoracic compressions. It is not necessary to stop thoracic compressions during breaths.

The foal should be in lateral recumbency. The foal should be moved to a firm, dry surface, if this has not been done already. The foal's rib cage should be palpated quickly and, if fractured ribs are suspected, the foal should be turned so that these are on the underneath side. The persons doing the thoracic compressions should kneel by the foal's spine and place their hands on top of each other, just caudal to the foal's triceps. Resuscitators should have their shoulders directly above their hands, enabling them to use their body weight to help compress the thorax (Figure 12.5-2). This helps reduce resuscitator fatigue.

The aim of thoracic compressions is not to squeeze blood out of the heart but rather to apply pressure to the whole thorax. Compression of the thorax is thought to re-



Figure 12.5-2 Resuscitation of a foal, illustrating ventilation with a resuscitation bag and nasotracheal tube and thoracic compressions.

sult in blood flowing forwards from the heart and the pulmonary vasculature. The pulmonary and aortic valves prevent backflow, and the atrioventricular valves do not play a role because pressure in the atria and ventricles are equal. The elastic recoil of the ribcage results in negative pressure in the thorax between compressions, allowing blood to fill the heart and pulmonary vasculature from the abdomen and head. Therefore to try and maximize the effectiveness of thoracic compressions, adequate time must be given for the vasculature to fill between compressions. A ratio of at least 1:1 compression to relaxation and preferably 1:2 is the goal.

Drugs

Drugs should be considered if the heart rate remains below 60 and is not increasing after 30 seconds of thoracic compressions and adequate ventilation. Thoracic compressions must continue after a drug has been given because all drugs require a circulation to reach the point of action, no matter what route they are delivered. The preferred route for drugs is intravenous. The jugular vein is usually obvious in foals and can be injected relatively easily, even with no circulation. If intravenous injection is not possible, drugs may be delivered either via the trachea or by intraosseous injection. For intratracheal administration, the needle of the syringe should be placed in the midline of the neck, through the skin and the ligament between two tracheal rings, below the level of the balloon of the nasotracheal tube, if present. An alternative method is to attach a dog urinary catheter to the syringe and pass the urinary catheter down the center of the nasotracheal tube so that the end is in the trachea. For intraosseous injection, a 14-gauge needle should be in the proximal medial one third aspect of the tibia or the radius. The needle is harder to place in the radius. The intratracheal dose of drugs may need to be higher than the intravenous dose, whereas the intraosseous dose is probably the same. Intracardiac injection should never be used because of the risk of laceration of a coronary artery or deposition of the

drug in the myocardium resulting in fibrillation. If drugs are required for resuscitation, the prognosis is poor.

The primary drug for resuscitation is epinephrine (adrenaline). The intravenous dose is 0.01 to 0.02 mg/kg, which is 0.5 to 1 ml of the 1 mg/ml (1:1000) solution for a 50-kg foal. Epinephrine should be given every 3 minutes until the return of spontaneous circulation, because it has a short half-life. The dose for intratracheal epinephrine is 0.1 to 0.2 mg/kg, which is 5 to 10 ml of the 1-mg/ml solution for a 50-kg foal. This higher dose should not be used intravenously, despite previous recommendations to the contrary, because it increases the risk of harm (intracranial hemorrhage), and no evidence exists that it offers any advantage. It also has been previously recommended to dilute epinephrine to 0.1 mg/ml (1:10000), based on practice for human neonates. This is also unnecessary, given the large size difference between human and equine neonates. Epinephrine increases vascular tone through activation of α -adrenoreceptors. This results in an increased aortic diastolic pressure, which increases blood flow through the coronary arteries and myocardium during the relaxation phase of thoracic compressions.

Volume expansion of the circulation is recommended for foals that have a poor response to resuscitative efforts, have weak pulses with a good heart rate, or remain pale or cyanotic after oxygenation. The initial expansion is achieved by use of 10-ml/kg balanced electrolyte solution (lactated Ringer's solution or Normosol-R) or 2 ml/kg hydroxyethyl starch (hetastarch 6% or pentastarch 10%). Fluids may be administered intravenously or intraosseously but not via the trachea. The fluids should be warmed to 100° F (38° C), if possible. Further fluid therapy may be required in the postresuscitation period. However, because of the risk of hypoxic ischemic encephalopathy in these foals (see Chapter 12.4: "Perinatal Asphyxia Syndrome in Foals"), further fluid therapy should be conservative. Careful monitoring of the effect of incremental boluses of 2 to 3 ml/kg of crystalloids or 0.5 ml/kg hydroxyethyl starch is recommended.

Sodium bicarbonate is a highly controversial treatment in neonatal resuscitation. The recommended dose is 0.5 to 1 mEq/kg, which is 50 to 100 ml of 4.2% solution (or 42 to 84 ml of 5% solution) for a 50-kg foal. It is not suitable for intratracheal administration. The theoretical indication for sodium bicarbonate is prolonged cardiopulmonary arrest that does not respond to other therapy and then only after effective ventilation is established. Its suggested role is to combat documented or presumed metabolic acidosis, caused by the build-up of lactic acid in prolonged arrest. However, conflicting data exist regarding its effectiveness in experimental cardiac arrest, and it may be counterproductive by initially decreasing intracellular pH. Sodium bicarbonate solutions more concentrated than 5% should be avoided, because of the risk of intracranial hemorrhage.

Drugs other than epinephrine and fluids should be used only in the case of documented cardiac dysrhythmias. This requires an electrocardiogram (ECG) machine, which is unlikely to be readily available in the field. Moreover, most human infants with serious dysrhythmias have sustained overwhelming cerebral injury in addition to cardiac injury, which suggests that newborn foals that develop a dysrhythmia may be unlikely to survive.

Atrial fibrillation, identified on auscultation as an irregularly irregular rhythm, occurs occasionally in the immediate postnatal period. These foals do not require immediate specific treatment. If the underlying heart rate is below 60 bpm and not increasing, or the foal meets any other criteria for resuscitation, as described above, then standard CPR should be instituted. These foals usually revert to sinus rhythm within a few hours of birth. Many normal foals may have arrhythmias for up to 15 minutes after birth, including wandering pacemaker, atrial premature contraction, and ventricular premature contractions. These dysrhythmias do not require specific treatment.

Asystole, recognized by the absence of cardiac electrical activity, should be treated with epinephrine as described above. Ventricular fibrillation, recognized by rapidly undulating electrical activity with no discernable complexes, is treated most effectively with an electrical defibrillator. The stimulus is 1 to 4 J/kg (50 to 200 J for a 50-kg foal), increasing the energy by 50% at each defibrillation attempt.

Bretium tosylate, a class 3 antidysrhythmic drug, has been reported to induce "chemical" defibrillation in dogs and man. It may be indicated, at a dose of 5 to 10 mg/kg (5 to 10 ml of the 50-mg/ml solution for a 50-kg foal), in foals with documented ventricular fibrillation when electrical defibrillation is not available. Lidocaine (lignocaine), a class 1b antidysrhythmic drug, is indicated in documented ventricular tachycardia. The formulation that does not contain epinephrine (adrenaline) should be used. Lidocaine should be administered at a dose of 1 to 2 mg/kg (2.5 to 5 ml of the 2% solution for a 50-kg foal), followed by an infusion at 20 to 50 μ g/kg/min. If the ventricular tachycardia is still present 20 minutes after the first bolus, a second bolus of the same dose should be given and the infusion maintained.

Atropine and calcium should not be used in CPR of newborn foals. Atropine has little effect if the bradycardia is not vagally mediated, increases myocardial oxygen consumption and may precipitate atrial and ventricular tachycardias. The recommended treatment for bradydysrhythmias is artificial ventilation and thoracic compressions. Although calcium improves the contractility of the normal heart, during cardiac arrest it leads to an increased cytosolic calcium concentration, which results in disruption of myocardial function.

MONITORING THE EFFECTIVENESS OF CARDIOPULMONARY RESUSCITATION

During CPR, monitoring the effectiveness of the resuscitative efforts can help adjust the technique to the individual patient. For example, the rate of ventilation, the rate and pressure of thoracic compressions, or the compression to relaxation ratio can be varied.

The pulse, if palpable, is the best way of monitoring thoracic compressions. The pulse can be felt in the carotid artery deep to the jugular vein in the neck or occasionally in the dorsal metatarsal artery between the cannon bone and the lateral splint. The progress of CPR can be monitored by the heartbeat, if present, which is used to decide when to stop thoracic compressions (see Figure 12.5-1). Although an ECG can be useful for monitoring the heart rhythm, it is not adequate for monitoring CPR, because electrical activity in the heart can continue without effective contractions (pulseless electrical activity).

CPR also can be monitored by the pupillary light reflex. Although slightly sluggish in newborn foals, it is present uniformly at birth. If the person doing the thoracic compressions keeps a flashlight (pen torch) in his or her mouth, he or she can then lean across and assess the pupil response and size without unduly interrupting the resuscitation efforts. The pupil is dilated widely and fixed if resuscitation is inadequate, whereas an adequate circulation results in a more normal pupil, which responds to light.

If the equipment is available, an end-tidal carbon dioxide monitor (capnograph) is useful to assess the effectiveness of CPR. The higher the expired carbon dioxide tension, the more effective the resuscitation efforts because more carbon dioxide is being transported to the lungs and removed by ventilation. End-tidal carbon dioxide tensions greater than 15 mm Hg indicate good perfusion and portend a good prognosis, whereas tensions persistently lower than 10 mm Hg indicate ineffective CPR and a poor prognosis. Muscle tone also increases with effective CPR.

A scoring system for assessment of foals in the immediate postnatal period, the modified Apgar score, has been published for foals. The usefulness of this score is unclear, because no data link the score and outcome of resuscitation. Furthermore, the first Apgar score is taken at 1 minute, a time at which resuscitation efforts already should have started for many foals.

WHEN TO STOP

Ventilation should be stopped when the heart rate is above 60, and spontaneous breathing is well established. This can be tested by stopping ventilation and disconnecting the bag or pump for 30 to 40 seconds and checking for a respiratory rate above 16 bpm, a regular respiratory pattern, and normal respiratory effort. Assisted ventilation may reduce the arterial carbon dioxide tension, and thus the respiratory drive; consequently, it may take as long as 20 seconds for spontaneous ventilation to start and the first few breaths may be gasping. A normal respiratory rate and pattern should follow. Premature withdrawal of assisted ventilation is reported to be the most common mistake in human neonatal CPR.

Once begun, thoracic compressions should be continued until a regular heartbeat of more than 60 has been established. Briefly stopping the compressions to assess whether a spontaneous circulation has been restored is necessary. In contrast to breathing, no lag period should occur between the stopping of support and the onset of a spontaneous heartbeat. Therefore, CPR should be stopped for no longer than 10 seconds to assess the circulation.

Clinical experience suggests that, if spontaneous circulation and respiration are not present after 15 minutes, then survival is unlikely. Spontaneous circulation and respiration rarely return in the absence of a pupillary light response or any other sign of forebrain activity. These foals appear highly unlikely to recover.

CARE OF FOALS AFTER RESUSCITATION

Foals that have been resuscitated continue to require support and should be monitored intensively for at least 30 minutes. Supplemental oxygen should be provided (start at 9 L/min), either by facemask or by nasal cannula. A careful physical

examination should be performed, and, if available, the heart should be monitored with an electrocardiogram.

The consequences of asphyxia during arrest and resuscitation can be serious and may not be apparent for 24 to 48 hours after the arrest. A syndrome of altered neurologic status, seizures, impaired gastrointestinal function, and impaired cardiovascular function can result. The term *hypoxic ischemic encephalopathy* (see Chapter 12.4: "Perinatal Asphyxia Syndrome in Foals") has been used to describe this condition because the neurologic signs are usually the most obvious. Previously it was known as *neonatal maladjustment syndrome*.

The effects of asphyxia are not preventable. Vitamin E and selenium (1 ml of 50 IU vitamin E/2.5 mg selenium intramuscularly q24h) act as free radical scavengers, which may reduce oxidative damage. Dimethyl sulfoxide (150 ml of 10% solution, slow intravenously q12h) acts as a free radical scavenger and reduces cerebral infarct volume in asphyxiated rats. These treatments may reduce the severity of signs, but no objective evidence in foals verifies this. Cerebral edema appears to be a particular risk in these foals, therefore fluid therapy should be conservative rather than aggressive and, where appropriate, colloids should be used instead of crystalloids.

The decision whether to refer a foal for intensive care is based on many factors, including availability and the costs versus the economic worth of the foal. Costs for intensive care vary markedly between hospitals, but were typically in the range of \$3000 to \$7000 in 2002 for foals with severe hypoxic ischemic encephalopathy. Success rates also vary but are approximately 70% to 80% for most units. Foals that have been resuscitated successfully are at high risk of complications, and referral should be considered strongly if circumstances allow.

NEW DIRECTIONS IN HUMAN CARDIOPULMONARY RESUSCITATION

Research in CPR is active in human medicine. Many innovations have led to a greater percentage of successful CPR (return of spontaneous circulation) but no change in the number of patients who ultimately leave the hospital. In the last 2 years, however, two treatments have been

shown to lead to increased hospital survival in human adult patients. In adult humans mild hypothermia (32° to 34° C; 89.6° to 93.2° F) induced by icepacks to the head and torso, or by blowing cold air over the entire body, for 12 to 24 hours after cardiac arrest results in better neurologic outcome and 6-month survival than conventional treatment. Shivering is controlled by pancuronium or vecuronium administration. These intriguing results may provide a way to limit hypoxic ischemic injury in resuscitated foals, but the use of muscle relaxants would necessitate mechanical ventilation and the results in neonates may be different from adults that have been studied.

Amiodarone (5 mg/kg intravenously) has largely replaced lidocaine as the preferred drug for ventricular tachydysrhythmias in human adult patients. These dysrhythmias are rare in the foal.

A further innovation in human CPR has been the introduction of vasopressin (0.4 to 0.8 U/kg intravenously) as a replacement or adjunct to epinephrine. However, the one experimental situation in which epinephrine is superior to vasopressin is in asphyxiated neonatal pigs. Therefore, pending further work, epinephrine remains the preferred drug for neonatal foals.

Supplemental Readings

- Corley KTT, Furr MO: Cardiopulmonary resuscitation in newborn foals, *Comp Cont Educ Pract Vet* 2000; 20:957-967.
- Furr M: Perinatal asphyxia in foals, *Comp Cont Educ Pract Vet* 1997; 18:1342-1351.
- Giles RC, Donahue JM, Hong CB et al: Causes of abortion, stillbirth, and perinatal death in horses: 3,527 cases (1986-1991), *J Am Vet Med Assoc* 1993; 203:1170-1175.
- Neonatal Resuscitation Program Steering Committee: Textbook of Neonatal Resuscitation, 3rd edition, Dallas, American Academy of Pediatrics/American Heart Association, 1994.
- Saugstad OD, Rootwelt T, Aalen O: Resuscitation of asphyxiated newborn infants with room air or oxygen: an international controlled trial: the Resair 2 study, *Pediatrics* [online], 1998 [<http://www.pediatrics.org/cgi/reprint/102/1/e1.pdf>].
- Yamamoto K, Yasuda J, Too K: Arrhythmias in newborn thoroughbred foals, *Equine Vet J* 1992; 24:169-173.

CHAPTER 12.6

Neonatal Septicemia

MARY ROSE PARADIS
North Grafton, Massachusetts

Septicemia in the neonatal foal is the most common cause of death in the first 7 days of life. The survival rate of septic foals has been cited to be between 37% and 55%. The challenges to the equine practitioner are early recognition of the risk factors that may predispose a foal to bacterial infection, early identification of the disease process, and early intervention to prevent the animal's condition from spiraling down into irreversible shock. To meet these challenges, the veterinarian must be aware of the normal physiologic events that occur during the perinatal period. Deviations from these events can result in devastating consequences to the foal.

EARLY RECOGNITION OF RISK FACTORS

The time period before, during, and after birth of an animal is generally considered the perinatal time. Maternal health during the perinatal period can directly influence the health of the foal. This is especially important during the prenatal period. Prenatal infections in the mare—such as pneumonia or enteritis/colitis—can enter the bloodstream and develop into septicemia. Hematogenous spread of the infection to the foal may occur.

The health of the placenta plays an important role in protecting the foal from possible infection. Conditions of the placenta that should be considered high risk for predisposing the foal to septicemia include placentitis and placental separation. Placentitis presents clinically as premature lactation and vaginal discharge in the mare. The presumed route of infection is the cervix. The most commonly encountered infectious agents include fungi and bacteria. *Aspergillus* is the most likely fungus cultured, whereas *Escherichia coli* and β -hemolytic streptococci are the predominantly recovered bacteria. The risk of septicemia in the fetus of the mare with bacterial placentitis is high. Infection can occur *in utero* as a direct extension of the placentitis. One study reported that 80% of aborted fetuses from mares with acute placental lesions were septicemic. Bacteria could be isolated from the fetal blood, lung, and stomach in these cases.

The clinical signs of placentitis—vaginal discharge and premature lactation—should alert the clinician to the other consequences of this disease. Besides the possibility of hematogenous spread of infection to the foal, the contaminated vaginal discharge may serve as a source of infection to the newborn foal as it passes through the birth canal during parturition. Premature lactation results in poor-quality colostrum for the foal at birth. Inadequate colostral antibody transfer, otherwise known as partial or complete failure of passive transfer (FPT), is the most common cause of septicemia after parturition.

The mare's placentation inhibits any *in utero* transfer of antibodies from the maternal to fetal circulation. Because the foal is born with no IgG and very little IgM, it is susceptible to infection. Colostrum is the first mammary secretion that the mare produces, and it is a distillation of IgG, IgGt, IgM, and IgA. Other factors in colostrum such as complement, lactoferrin, lymphocytes, and CD14 seem to factor in the immunologic protection of the foal.

The mare begins colostrum production approximately 3 weeks before parturition and it is only made once. Good-quality mare colostrum contains IgG levels ranging from 4000 to 6100 mg/dl. Extensive premature lactation has the effect of diluting the colostral antibodies to that of normal milk secretion, less than 2000 mg/dl IgG.

Premature placental separation can indirectly increase the risk of the foal's developing septicemia. If the placenta separates during parturition, the foal may experience a period of asphyxia. This lack of oxygen may produce a foal that is neurologically compromised and thus unable to stand and nurse after parturition. Ingestion of good-quality colostrum must occur within the first 8 to 10 hours after birth. This is the period when the gastrointestinal tract is most receptive to the absorption of the large molecular weight immunoglobulins.

Acceptable levels of antibody transfer in foals range from 500 to 800 mg/dl. The age of the mare may play a part in determining the quality of colostrum. Foals born to older mares have an increased risk of not achieving immunoglobulin levels of more than 800 mg/dl. Low environmental temperatures and a decreased amount of solar radiation may also negatively affect colostral and foal serum IgG levels.

Not all foals with low immunoglobulins become septic. Management and environmental factors also play a role in the susceptibility of the foal to infection. Foals that are born into or raised under unsanitary conditions are at higher risk than foals that are born on well-managed farms. Cleaning the mare's udder and legs before the foal begins to udder seek may decrease the bacterial load to which the foal is exposed.

EARLY RECOGNITION OF SEPSIS

Early recognition of sepsis is imperative to the successful outcome of the foal. It is not hard to diagnose septicemia in the foal that is presented in septic shock. These animals are recumbent and often unaware of their surroundings. They have decreased cardiac output and hypotension that manifests as cold extremities, cyanotic mucous membranes, prolonged capillary refill time, and weak to absent periph-

eral pulses. The degree of hypotension can roughly be determined by the sequence of loss of peripheral pulses. The more peripheral pulses are the first to be lost. For example, a septic foal would lose the greater metatarsal artery pulse first and later the femoral pulse as shock progresses.

The greater challenge comes in recognizing the early signs of sepsis to prevent irreversible shock. These signs can be subtle and variable in each foal. The importance of a thorough perinatal history (see Chapter 12.1: "Evaluation and Early Care of the Sick Neonatal Foal") and physical examination cannot be overstressed. Clues in the history that may be predictive of sepsis include premature lactation, vulvar discharge, prenatal illness in the dam, dystocia, a delay in time of standing and nursing in the foal, and foal rejection by the dam. All of these factors should raise the clinician's level of suspicion that this foal may develop a problem.

The practitioner's examination of the foal should begin with observation of the foal's behavior. The normal neonate should be vigorous and active soon after birth. Soon after the foal is expelled from the birth canal, it should position itself in sternal recumbency. Within the first hour of life the foal should be scrambling around the stall and making attempts to stand. At this time the foal should also be making suckling motions with its tongue. The normal foal should be standing and nursing by 3 hours of life. Any deviation from this pattern may indicate the possibility of an *in utero* infection. If infection is not already present, this foal may be predisposed to postnatal infection caused by delayed colostral ingestion.

One of the first consistent signs of developing sepsis in the newborn foal is depression and lethargy. Owners may report that their foals are quiet, easy to handle, and appear to sleep most of the time. Normal foals in the first week of life nurse approximately five to seven times an hour in short 30- to 90-second bursts. The sick foal often has a decreased or absent suckle reflex. A distended and leaking mare's udder may indicate that the foal is not nursing as often as it should.

Dehydration or hypovolemic shock may be difficult to determine in the sick equine neonate. Tenting of the skin is unreliable because even in the normal foal it remains tented when pinched. The packed cell volume (PCV) and total protein levels (TP) in foals are normally lower than in the adult; therefore, significant increases for a particular foal may be underinterpreted in comparison to adult values. The best indicators of dehydration in foals are tacky mucus membranes and the presence of sunken eyes. Septic foals quickly lose fluid and fatty tissue behind their eyes. As the globe of the eye retracts in the socket, the foal often develops entropion of the lower lid. This can develop rapidly and is often seen in sick foals younger than 24 hours of age.

Other clinical signs of sepsis vary. The presence of a fever or hypothermia would certainly be cause for concern, but an equal number of septic foals present with a normal temperature. Mucus membranes may be pale, congested, or gray with or without petechiae in the septic newborn. Because of the systemic nature of the disease, many different organs may be involved and present their own set of clinical signs.

The lungs are the most commonly affected organ sys-

tem in the septic foal. Early clinical signs may include an increased respiratory rate and effort. Auscultation of the lungs of a newborn foal is not always helpful in determining the presence of disease. If the examiner hears crackles or wheezes on auscultation, it is certain that the lungs are involved, but quiet lung sounds do not ensure a normal respiratory system. Consolidation of the lungs may be present despite normal findings on auscultation. Hypoxemia is often present in foals with respiratory compromise. Approximately 83% of septic foals in one study experienced mild to severe hypoxemia. Unfortunately, the observation of cyanotic mucus membranes does not occur before the P_{aO_2} is less than 40 mm Hg. In the newborn foal with severe respiratory compromise, hypercapnia with P_{aCO_2} greater than 50 mm Hg can develop.

Because of the previously stated reasons, thoracic radiographs and arterial blood gas analysis should be considered important diagnostic adjuncts in the examination of the foal that one suspects is septic. Most portable x-ray units can be used to image the newborn foal's lungs with the use of rare earth screens. Portable blood gas machines are now available and can be used by the ambulatory veterinarian to determine the degree of hypoxemia or hypercapnia. The lateral metatarsal artery is a good place to obtain an arterial blood sample except in the hypoperfused foal.

The second most common system failure presented in septic foals involves the gastrointestinal tract. Enteritis or colitis may occur as a result of ingestion of an infectious agent or through hematogenous spread of bacteria. Clinically this may present as ileus, abdominal distention, colic, and/or diarrhea. Radiography, ultrasonography, and abdominocentesis may be helpful in ruling out other causes for these clinical signs—such as intussusception, volvulus, and bladder rupture.

Other less common but equally devastating manifestations of sepsis in the foal include meningitis and septic arthritis. Foals that present with septic meningitis have a severely depressed mentation that may be accompanied by seizure activity. The affected animals may hold the head and neck in a rigid position and exhibit extensor rigidity of the forelimbs. Focal signs may include strabismus, head tilt, and nystagmus. One of the difficulties in diagnosing septic meningitis is that it mimics many of the clinical signs that are common to neonatal maladjustment syndrome. The diagnosis depends on a cerebrospinal fluid (CSF) analysis. A CSF sample can be taken fairly easily from the lumbosacral space of a recumbent foal using a 1.5-inch, 20-gauge needle. An increased number of white blood cells with the presence of any neutrophils in the CSF should point toward a diagnosis of septic meningitis.

Lameness or joint effusion present in an equine neonate should be diagnosed as septic arthritis or osteomyelitis until proved otherwise. Septic arthritis was a clinical feature of 28% of the septic foals in one study. Osteomyelitis may be present without overt signs of joint swelling. The first clinical observation may be that the foal appears to spend most of its time recumbent, which indicates bone or joint pain. Careful palpation of the joints and the bone proximal to the physal regions of the long bone should be part of the physical examination.

Diagnosis is facilitated by radiography of the suspected

bone or joint and by arthrocentesis. Osteomyelitis may be seen as lytic areas in the bone in the region of the physis or epiphysis. Bony lesions may not be radiographically evident in the beginning of the course of the disease but develop over the period of a week. For this reason it is important to radiograph the suspicious joint every 5 to 7 days if the foal is not responding to therapy.

Arthrocentesis of a septic joint will yield synovial fluid with an elevated white cell count (>500 cells/ μ l) with neutrophils predominating on cytology. Infection of a joint results in the fluid becoming less viscous. The synovial fluid can be crudely tested in the field by putting a drop on the thumb and forefinger and observing whether a string of fluid forms when the fingers are pulled apart. In the septic joint, synovial fluid is watery and will not form this stringiness.

Foals with septic arthritis or osteomyelitis tend to spend more time recumbent than a healthy foal. For this reason they are more prone to develop decubital ulcers over the bony prominences of the shoulder, elbow, hock, stifle, and hip. The first sign of the decubitus is a change in the skin texture from soft and pliable to stiff and leathery. This devitalized skin eventually sloughs and leaves raw, open wounds.

Umbilical remnant infections have been incriminated as a source of the widespread infection that constitutes septicemia. In one study, 25% of the total number of foals that were classified as septic had umbilical infections. Interestingly, if the foal had septic arthritis or osteomyelitis, its chances of having an umbilical infection increased to 50%. External examination of the umbilicus of a foal is important, but it does not completely rule out the possible presence of internal infection. Ultrasonography of the internal structures of the umbilical remnant is important in determining the source of the infection. Structures that should be examined and measured include the umbilical stalk and vein, the two arteries, and the urachus. Enlargement of any of these structures over normal values indicates infection.

Laboratory Investigation

Some basic clinical laboratory tests are also very useful in confirming the diagnosis of sepsis. Complete blood count (CBC), blood glucose level, serum chemistry profile, arterial blood gas analysis and immunoglobulin determination constitute a good minimal database. A leukopenia represented by a neutropenia is the most common white blood cell abnormality is seen in the septic foal. The clinical pathologist may also note toxic changes in the neutrophil. Leukocytosis may be seen in foals that have a persistent infection, such as a septic joint.

Septic foals younger than 24 hours of age are often hypoglycemic as a result of their failure to nurse and their lack of glycogen storage. The newborn foal has only enough glycogen to maintain blood glucose in the normal range for 2 to 3 hours without the ingestion of colostrum. Nutritionally, colostrum is more calorie-dense than mare's milk. Ingestion of adequate colostrum will maintain the foal's glucose in the normal range for up to 19 hours.

Because neonatal sepsis has a close association with

failure of passive transfer of colostral antibodies, serum IgG levels should be determined in all questionably sick equine neonates. Several field tests are available to evaluate serum immunoglobulins. Two of the more common kits used are the zinc sulfate turbidity test and an enzyme-linked immunosorbent assay (ELISA) test. The latter test takes only 7 minutes to perform and can be used on whole blood, plasma, or serum. The gold standard test for IgG is a radioimmunoassay test. The problem with this test is that it takes 12 to 24 hours to read the results (see Chapter 12.3: "Immunodeficiencies of Foals").

The taking of blood cultures is advocated in cases of neonatal septicemia because a high number of confirmed septic foals have a positive blood culture. The problem of relying on blood cultures to confirm a diagnosis of sepsis is that it may take 72 hours or more before the results are available. The need to determine the presence of sepsis is immediate. Because of this need, a sepsis scoring system has been designed. A sepsis score is determined by entering particular historical information, physical examination, and clinical pathologic parameters into the system (Table 12.6-1). Specific points are assigned to these parameters and a score is calculated. Foals with scores of less than 11 are generally not septic. The sepsis score has proved to be a useful clinical tool, but because it is not 100% reliable, a strong clinical suspicion of sepsis should lead one to treat the foal despite a low score.

EARLY INTERVENTION STRATEGY

The key to a successful outcome when confronted with the possibility of a septic foal is prevention or early intervention. The treatment of prepartum mares with clinical signs of infectious placentitis includes the use of appropriate systemic antibiotics and antiinflammatory agents. Stall rest may also be important for prolonging gestation. The antimicrobial agents should be chosen on the basis of results of cultures done on the uterine discharge. Late pregnancy in females lowers the plasma concentrations of some drugs by 10% to 50%, but the way in which antimicrobial distribution is altered in the pregnant mare remains unknown. Studies on the transfer of antimicrobials across the normal equine placenta have compared trimethoprim/sulfa, penicillin, and gentamicin. Trimethoprim/sulfa was the only one of these three drugs that could be detected in fetal fluids. In addition, placentitis may alter these dynamics.

If significant premature lactation has occurred during the prepartum period, the mare's mammary secretion should be analyzed for immunoglobulin content at the time of parturition. Two stallside methods with specific instruments calibrated to measure specific gravity of mare's colostrum can make the analysis. The specific gravity of the secretion is correlated to IgG concentration. A high specific gravity indicates a high concentration of IgG. If the colostrum is of low quality, the foal should be given one liter of colostrum of a known quality from another mare, or it should receive a plasma transfusion soon after birth. When the risk of sepsis is high, prophylactic antibiotics should be considered.

In foals that are already showing signs of septicemia, the general goals are to rid the animals of the offending organism through immunologic and antimicrobial sup-

Table 12.6-1
Modified Sepsis Score

Foal's Name _____	Date _____	Total Score _____
Case # _____	Check One:	
	_____ At admission?	
	_____ Day subsequent to admission?	
	Indicate day #: _____	

Information Collected:	4	3	2	1	0	This Case
CBC						
Neutrophil count		<2000/mm ³	2000-4000 or >12,000	8000-12,000	Normal	
Band neutrophil count		>200/mm ³	50-200		<50	
Doehle bodies, toxic, granulation, or vacuolization in neutrophils	Marked	Moderate	Slight		None	
Fibrinogen			>600	500-600	≤400	
Other Laboratory Data						
Hypoglycemia			<50 mg/dl	50-80	>80	
Immunoglobulin	<200	200-400	401-800		>800	
Clinical Examination						
Petechiae or scleral injection not secondary to eye disease or trauma		Marked	Moderate	Mild	None	
Fever			>102° F	<100° F	Normal	
Hypotonia, coma, depression, convulsions			Marked	Mild	Normal	
Anterior uveitis, diarrhea, respiratory distress, swollen joints, open wounds		Yes			No	
Historical Data						
Placentitis, vulvar discharge before delivery, dystocia		Yes			No	
Prematurity (days)		<300	300-310	310-330	>330	
						TOTAL POINTS _____

From Brewer BD, Koterba AM: Development of a scoring system for the early diagnosis of equine neonatal sepsis. *Equine Vet J* 1988; 20(1):18-22.

A score of 11 is used as the cut-off point in determining nonseptic (<11) or septic (≥11) foals.

port and to prevent the endotoxin released from the bacteria from starting the cascade of irreversible shock.

Immune Therapy

Virtually all septicemic foals have FPT (IgG <800 mg/dl). Exceptions may be those foals that were infected *in utero* but received adequate colostrum at birth. Plasma transfusions are routine in attempting to provide immunologic support for these animals. Immunoglobulins opsonize bacteria, which facilitates phagocytosis by neutrophils. Although transfused plasma does not provide the same level

of protection as good-quality colostrum, its contribution in the sick foal is important.

In general, the aim of the plasma transfusion is to raise the foal's IgG level up to 800 mg/dl. IgG levels in the normal foal increase at a rate of 20% of the concentration of the transfused plasma for each liter transfused. For example, if 1 L of plasma contains 1000 mg/dl of IgG, the expected rise in immunoglobulin in the foal is 200 mg/dl. The percentage rise in immunoglobulin decreases in the sick foal to approximately 11% of the transfused immunoglobulins. This decreased rise in the sick foal may be caused by rapid consumption of the immunoglobulins by

the infection or may be caused by sequestration in the extravascular space or areas of inflammation.

Other forms of immunotherapy have been used or are currently being investigated. Hyperimmune serum with antibodies against the rough mutant of *Salmonella* or *E. coli* is used clinically in some neonatal intensive care units as an antiendotoxin therapy. Some commercially available plasma has been obtained from mares that are vaccinated against *E. coli* J5 and/or *Salmonella typhimurium*. Antibodies from these agents are thought to block the attachment of endotoxin to CD14, which initiates cascade of interleukins and tumor necrosis factor.

Various forms of lyophilized or monoclonal antibodies can be used as an oral supplement to colostrum of questionable quality. Care should be taken in relying on these products as the sole source of immunoglobulin. They are intended as supplements. Colostrum has other factors in addition to IgG that are important to the health of the neonate. Complement, growth factors, cytokines, and lactoferrin are also present and seem to play an important role in the passive immunity of foals.

Antibiotic Therapy

Appropriate antibiotic therapy is important in the elimination of the bacterial infection of the septic foal (see Chapter 1.1: "Neonatal Pharmacology and Therapeutics"). Antibiotics should be administered immediately when the foal is suspected of being infected. This means that the practitioner is often asked to make a choice of antibiotic without culture results. Septic foals should be placed on broad-spectrum bactericidal antibiotics that are effective against gram-positive and gram-negative organisms.

Many retrospective studies have considered the types of bacteria present in septic foals. The most common gram-negative organisms include *E. coli*, *Klebsiella*, *Enterobacter*, *Actinobacillus*, *Pseudomonas*, *Citrobacter*, *Actinobacter*, and *Salmonella* species. The most common gram-positive organism cultured is *Streptococcus* species. In a study that involved 53 septic foals, 50% of the foals had a mixed gram-positive/gram-negative infection, and 50% of the foals were infected with a single organism. Approximately 89% of all the gram-positive organisms were cultured in a mixed infection along with a gram-negative organism.

The sensitivity patterns for these organisms have changed over the past 10 years, probably because of increased resistance developed by the organisms to some of the more commonly used antibiotics. Studies suggest that amikacin and cefotaxime are the most effective in killing the gram-negative organisms found in neonatal sepsis. Two commonly used antibiotics—gentamicin and trimethoprim/sulfa—have lower sensitivity patterns. Ampicillin and penicillin are still effective in killing *Streptococcus* species. Therefore an appropriate choice to initiate antibiotic coverage may include amikacin and ampicillin. Alternative antibiotic combinations should be considered when culture results are available or if the animal does not appear to be responding (Table 12.6-2).

Fluid Therapy

The gram-negative bacteria that are found in neonatal septicemia contain endotoxin in their cell walls. Release of

endotoxin in the animal initiates a cascade of cytokines that are responsible for many of the behavioral, hematologic, and hemodynamic changes that are seen in septic shock. The most important treatment strategy for diverting the lethal effects of endotoxin involves intravascular fluid expansion. Physiologically balanced crystalloid fluids—such as Ringer's, Ringer's lactate, or acetate—remain in the intravascular space three times longer than dextrose and water solutions; therefore these types of fluid would be favored in the treatment of septicemia. If the foal is hypoglycemic, dextrose may be added to the crystalloid solution; 100 ml of a 50% dextrose solution may be added to 900 ml of lactated Ringer's solution. This will make the solution a 5% dextrose concentration.

Because foals have a larger volume of distribution, their normal maintenance fluid requirements are higher than those of an adult horse—approximately 80 to 120 ml/kg per day or 3 to 5 ml/kg per hour. In the 45-kg foal, this translates to 3.6 to 5.4 L/day. The foal in septic shock may initially require a higher rate of fluids to combat the hypotension of endotoxemia. A shock dose of fluids would be approximately 20 ml/kg over 20 minutes. This dose can be repeated until the animal's condition is stabilized. For example, a 50-kg foal that has only a slight peripheral pulse, tacky mucus membranes, and sunken eyes, would receive 1 liter of crystalloid fluids in the first 20 minutes.

If no improvement was noted, a second and third liter would be administered. Urinary output should be monitored during fluid administration. Most foals urinate after approximately 3 L. If this does not occur, one should be suspicious of renal shutdown or a ruptured bladder.

If the foal has decreased peripheral pulses, cold limbs, depression, and anuria, the foal is probably hypotensive. Pressor/inotropic drugs may be indicated to increase perfusion. Dopamine (5-10 $\mu\text{g/kg}$ per minute), dobutamine (5-40 $\mu\text{g/kg/min}$), epinephrine (0.1-3 $\mu\text{g/kg/min}$), and norepinephrine (0.05-2 $\mu\text{g/kg/min}$) can be used in a continuous rate infusion to help increase the foal's blood pressure. A mechanical pump designed to achieve the optimum drug levels best delivers this therapy.

Specific System Therapy

Different manifestations of the septic process have specific therapy that is necessary for a successful outcome. Umbilical remnant infections may require surgical removal. Once the foal's condition is stable enough to undergo general anesthesia, the umbilical structures are carefully dissected. Enlarged or discolored structures should be removed. Culture of these tissues is often rewarding in determining the causative organism of the septicemia.

Septic Arthritis

Specific intraarticular therapy for septic arthritis is critical. Infection in or around a joint results in a rapid influx of inflammatory cells into the synovia. Cell counts can range from 10,000 to greater than 150,000 with protein levels increased above 2.5 mg/dl. The cells and their inflammatory byproducts are very damaging to cartilage cells. Multiple joint lavages with sterile lactated Ringer's solution are very effective in establishing a more normal synovial fluid. Joint flushes should continue on alternate days until joint fluid analysis results approach normal values. An-

Table 12.6-2
Antimicrobial Drugs Used in the Treatment of Equine Neonatal Septicemia

Drug Interval	Route	DOSE (mg/kg)	
		Amount	Frequency
amikacin sulfate	IV, IM	20-25	Once daily
gentamicin sulfate	IV, IM	6.6	Once daily
cefotaxime sodium	IV, IM	15-25	q12h, q8h
ceftiofur*	IV,* IM	4.4-10	q12h/q6h
penicillin G sodium	IV	20,000-40,000 IU/kg	q6h
ampicillin sodium	IV, IM	10-15	q6h
ticarcillin sodium	IV, IM	40-60	q8h
ticarcillin-clavulanate	IV	50	q8h, q6h
trimethoprim-sulfonamide	PO	15-30	q12h

IV, Intravenous; IM, intramuscular; q12h, every 12 hours; PO, by mouth.

*Ceftiofur, given intravenously, should be administered slowly over 20 minutes to prevent rapid renal elimination.

tibiotics, in particular amikacin, instilled into the joint after flushing will achieve high intraarticular concentrations of the antimicrobial. In treatment of human septic arthritis, a delay of treatment by more than 48 hours has been found to significantly worsen the prognosis.

Arthroscopy may be required if a large amount of fibrin is in the joint. This procedure would also allow for visual assessment of the joint cartilage. Osteomyelitis may require surgical debridement of the infected bone. Regional perfusion of antibiotics can be accomplished in the limb by placing a tourniquet above the joint that is affected. Antibiotics are delivered through a catheter in the venous system of that joint. The high pressures in the venous system allow the antibiotics to diffuse into the surrounding tissues over a period of 20 minutes, thus achieving high levels of antimicrobial locally.

Pneumonia

Septic foals that present with bacterial pneumonia may progress into respiratory failure with P_{aO_2} less than 60 mm Hg and P_{aCO_2} higher than 55 mm Hg. These foals require intensive respiratory physiotherapy that consists of oxygen administration and mechanical positive pressure ventilation until the antibiotics and immunologic supports can have a chance to work. This is extremely labor-intensive work best performed at an intensive care facility. Hypoxia without hypercapnia often responds to oxygen supplementation. Oxygen can be administered through a facemask or an in-dwelling nasal oxygen tube.

Corneal Ulceration

Corneal ulceration is often a secondary problem associated with the septic foal. As stated previously, the eyes of the septic foal often become sunken as the result of dehydration and loss of the infraorbital fat. The common consequence of this retraction of the globe is entropion of the lower lid. The entropion produces irritation and ulceration of the cornea. Aggressive therapy of these ulcers is important. Topical ophthalmic antibiotics should be placed in the eye four to five times a day. The entropion is easily

corrected by placing a temporary mattress suture in the lower lid and rolling the eyelashes away from the cornea.

Nutritional Support

The normal, healthy 45-kg foal ingests approximately 12 to 13 L/day of mare's milk. This provides about 130 to 150 kcal/kg per day (5850-6750 kcal/day). For the first week of life a normal foal feeds on the average five to seven times per hour for short periods. If nutrition is not a prominent component of the strategic therapeutic plan for the septic foal, hypoglycemia, loss of lean body mass, and malnutrition become a problem. Malnutrition compromises the healing process of the foal. Chemotaxis of white cells, complement levels, T cell activity, and wound healing all decrease.

Nutritional assessment of a foal should include the assignment of a body score (1 = extremely emaciated, 5 = normal), the recording of total intake of nutrition, and daily weighing of the foal. Healthy foals should gain 1 to 1.5 kg of body weight per day. Most foals double their birth weights in the first month of life. Sick foals tend to not gain weight or to actually lose weight during the period of their illnesses for several reasons. Illness itself may increase the caloric needs of the foal, but this is not always the case. The sick foal is generally less active than the healthy foal and therefore may have lower energy needs. The most likely cause for lack of weight gain is insufficient calorie ingestion because of illness or because care givers cannot provide sufficient calories through the methods described in the following discussion.

If the foal has a good suck reflex, it should be encouraged to suck from the mare. This is the least labor-intensive method of providing nutrition. Often the sick foal is uninterested in suckling. An in-dwelling nasogastric tube may be placed in foals that are anorectic. Attempting to administer 5000 to 6000 kcals (10-12 liters of milk) to a sick foal can be challenging. Generally, small amounts (200-500 ml) of mare's milk or milk substitute should be administered every 1 to 2 hours. This can be very labor-intensive and can

result in overloading the stomach with a large bolus of fluid. A more physiologic way to administer milk through a nasogastric tube would be by continuous rate infusion. This is easiest in the recumbent foal and avoids the periodic overloading of the stomach. A mechanical pump facilitates this process.

Providing adequate nutrition through enteral means only may become difficult. The presence of diarrhea or milk intolerance may further complicate the nutritional support of the sick foal. It is important for the health of the gastrointestinal tract to maintain some form of enteral nutrition, but partial parenteral nutrition (PPN) may need to be introduced to the patient. Glucose, amino acids, and lipids are the major components of parenteral nutrition. Vitamins, electrolytes, and trace minerals can also be added.

When considering the use of parenteral nutrition in the critically ill foal, one needs to weigh the advantages and disadvantages. The advantages are obvious in that one can provide the foal with a higher level of nutrition than through enteral formulations alone. Mortality rates in humans with multiple organ failure are significantly higher in those patients with a negative nitrogen balance. The disadvantages of TPN are numerous. They include catheter-related problems, labor intensity, hyperglycemia, and expense. Ideally, the foal should have a sterile central venous catheter that is dedicated to the TPN solution only. Technically, a constant infusion pump is needed to deliver the solutions at a constant rate. A veterinarian should be available to monitor the patient and its blood work at frequent intervals. The cost per day of parenteral nutrition varies with the formulations but ranges from \$75 to \$150 per day.

Calories for energy can be provided by the dextrose and lipid solutions. One gram of dextrose contributes 4 kcals of energy, whereas 1 gram of lipid provides approximately 9 kcals of energy. Using these components to make up the entire energy requirement of approximately 100 to 150 kcal/kg per day in the foal is important. This allows the amino acid solution to be used for protein building rather than as an expensive source of energy calories. This can be accomplished by keeping 100 to 200 nonnitrogen calories/g of nitrogen from amino acids.

Although 50% dextrose has been the traditional source of energy in TPN solutions, the addition of exogenous lipid has been helpful in many ways. It is an isotonic solution; therefore it lowers the hypertonicity of the solution, which in turn decreases the incidence of phlebitis. One guideline states that the lipids should not exceed 60% of the nonprotein calories.

To begin total or partial parenteral nutrition, it may be advisable to start by providing half the energy needs. As the animal adjusts to the high glucose levels, the energy and protein levels can be increased to the animal's full needs. A simple starting formula includes the following:

10 g/kg per 24 hours of glucose, 2 g/kg per 24 hours of amino acids, and 1 g/kg per 24 hours of lipid. The foal would receive approximately 53 kcal/kg and 140 non-protein calories per gram of nitrogen. Practically, for the 50-kg foal, this translates to 1 L of 50% dextrose, 1 L of 8.5% amino acids with electrolytes, and 0.5 L of 10% lipid with an approximate cost of \$70.

Blood and urine glucose should be measured two to three times a day for foals that are receiving parenteral nutrition. Most foals adjust to the glucose load within the first 24 hours if they are begun on a lower dose at a slow rate. Blood glucose levels that are consistently higher than 250 mg/dl may indicate glucose intolerance. If a further lowering of the glucose concentration does not alleviate the problem, insulin can be started along with the parenteral nutrition.

CONCLUSIONS

Despite the fact that treatment strategies for working with the critically ill foal have become more successful over the last 15 years, sepsis remains a serious cause of mortality in the equine neonate. Better identification of the high-risk mare and foal will enable practitioners to anticipate problems before they happen and to work toward their prevention. Developing a team approach with the owner, practitioner, and intensive care facility can improve the prognosis for the septic foal.

Supplemental Readings

- Barton M: Endotoxemia. Proceedings of the Dorothy Havemeyer Foundation, Neonatal Septicemia Workshop 3, pp 6-11, Talloires, France, 2001.
- Brewer BD, Koterba AM: Development of a scoring system for the early diagnosis of equine neonatal sepsis. *Equine Vet J* 1988; 20(1):18-22.
- Henson S, Barton M: Bacterial isolates and antibiotic sensitivity patterns from septicemic neonatal foals: a 15 year retrospective study (1986-2000). Proceedings of the Dorothy Havemeyer Foundation, Neonatal Septicemia Workshop 3, pp 50-52, Talloires, France, 2001.
- Koterba AM, Brewer BD, Tarplee FA: Clinical and clinicopathological characteristics of the septicemic neonatal foal: review of 38 cases. *Equine Vet J* 1984; 16:376-382.
- Paradis MR: Update on neonatal septicemia. *Vet Clin North Am Equine Pract* 1994; 10(1):109-135.
- White SL, Henson S, Barton M: The sepsis score revisited. Proceedings of the Dorothy Havemeyer Foundation, Neonatal Septicemia Workshop 3, pp 13-15, Talloires, France, 2001.
- Wilson WD, Madigan JE: Comparison of bacteriologic culture of blood and necropsy specimens for determining the cause of foal septicemia: 47 cases (1978-1987). *J Am Vet Med Assoc* 1989; 195:1759-1763.

CHAPTER 12.7

Angular Limb Deformities

TOM YARBROUGH

Sacramento, California

Most foals are born with some degree of angular deformity. The clinician's job is to evaluate the site, degree, and type of deformity, and while keeping in mind the owner's expected goals for the animal, outline management for the deviation. Angular deformities are characterized by how the limb deviates distally to the deformity. Valgus deformities denote lateral deviation (knock-kneed), and varus deformities describe medial angulation (bow-legged). These angular deviations may affect any section of the appendicular skeleton; the most commonly recognized deviations involve long bones with minimal overlying musculature (radius, tibia, metacarpus III, metatarsus III). These site predilections most likely represent a combination of regional susceptibility to disparate growth, a high degree of postpartum growth potential, and the fact that the deviation produced is more strikingly obvious when it involves a joint between two easily defined long bones.

Limb deformities can be classified as congenital or acquired; rotational or angular; involving the periarticular soft tissues, diaphyseal, epiphyseal, or metaphyseal sections of long bones; or involving cuboidal components of the skeleton. Any combination of these variables may be present in a given patient. An attempt should be made to assess the entire effected limb to avoid correction of the most striking deviation only to identify secondary defects after correction of the original presenting complaint. This is particularly important when we consider that the most apparent deviation may involve a section of the limb with a high degree of reserve growth potential, whereas the less apparent secondary problem might be in an area that must be addressed quickly—during the first few weeks of life—if any correction is to be obtained.

ETIOLOGY

Most of the proposed causes of angular limb deformities are purely speculative and offer little help to the clinician in correcting the problem nor to the owner in preventing future problems. Overweight mares, plant toxins, fetal malpositioning, colic, and placentitis have all been speculated to play a role. Any condition that results in a weak, premature, or dysmature foal can result in angulation of the limbs. In the postpartum period angulation is generally the result of abnormal stresses that alter the rate of growth of the physis or crushing of the developing cuboidal bones. This scenario can be set into motion by an unrecognized ligamentous laxity or incomplete ossification of the cuboidal bones, soft tissue injury, disparate weight bearing due to a neurologic or musculoskeletal abnormality in the contralateral limb, or poor hoof confor-

mation and care. The primary exception to the common postpartum causes of angular deformities is nutritional imbalance. Care should always be exercised in assessing the potential problems associated with excessive protein intake—such as physitis and mineral imbalances (such as copper deficiency or zinc toxicity)—that could lead to alterations in endochondral ossification.

ASSESSMENT

A complete assessment of the foal with angular deformities is imperative to a successful outcome. However, no truly defined parameters exist for complete assessment. Management of each case should be tailored to address the age, breed, and desired function of the animal as well as to the financial constraints of the owner.

Visual Inspection

Visual inspection is generally the first step in assessing deformities. As previously mentioned, care should be taken to evaluate all sites of potential angulation because foals commonly have multiple sites of deviation. Watching the limbs in flight will help determine the net effect of multiple deviations on the use of the limb. If rotational anomalies are a component of the deformity, placing markers on the limbs and watching the animal in motion is sometimes useful. This is a very subjective test but can provide some information once the clinician becomes familiar with the technique.

This author performs the test by placing strips of white tape at the palpable dorsal midpoint of the coronary band, distal metacarpus/metatarsus, distal radius or distal tibial physis, and bicipital tendon. With tape in place, determination of which deviations persist during foot flight is easier. Rotational deformities that originate high in the limb (elbow, shoulder) are very common and generally self correct as the foal matures and increases the width of its chest. Rotational deviations originating distal to the carpus usually require aggressive foot care or surgical intervention to correct. In addition, the visual examination should include evaluation of supporting limb deviations that may develop as a result of lameness.

Physical Examination

Physical examination of the foal is generally most important in the early postpartum period. Assessment should concentrate on determining the strength of the periarticular fibrous support structures and maturity of the foal. Standardbreds and draft breeds are often affected with deviations

secondary to ligamentous laxity; however, these deviations rarely persist for more than a few days, except in animals that have been recumbent or aggressively splinted. The degree of ligamentous laxity can be assessed by manipulation of the long bones adjacent to the deformity to determine if manual realignment is possible. It should be noted that foals born with significant deformities from contracture of the superficial digital flexor tendons often have the appearance of significant laxity of the collateral supporting structures of the metacarpophalangeal/metatarsophalangeal joints, which will resolve once the contracture is resolved.

Radiographic Evaluation

Radiographic evaluation is most important in the early postpartum period to assess the degree of incomplete ossification of the cuboidal bones and the risk of performance limiting collapse. Complete examination via radiography requires at least two orthogonal views to determine the degree of ossification and angulation as well as to provide a baseline for assessment of the response to therapy. With the exception of foals with incomplete ossification of the cuboidal bones, radiographs primarily provide a record of the site and degree of angulation but rarely alter the treatment plan developed during the physical examination. Radiographic assessment of the degree of angulation has been determined by two techniques. The first involves radiographic plates long enough to image the middiaphysis of the long bones on either side of a deviation. With this information captured on film, drawing a line down the diaphysis of each longbone is possible. The point of bisection of these two lines gives both the net focus of deviation and angle of deviation. The second technique is most commonly used in angular deformities that involve the carpus and can be performed on radiographs imaged on smaller film. With this technique, lines are drawn parallel to the physis and the articular surfaces of the three carpal joints. Sites where these lines deviate from parallelism demonstrate the points of deviation.

TREATMENT

Periarticular Ligamentous Laxity

In cases of severe ligamentous laxity in the neonate, efforts must be made to protect the developing cuboidal bones. If the laxity is allowed to persist, uneven weight bearing can cause damage to even normally developed carpal and tarsal bones. The form and duration of support must be closely managed to reduce the possibility of secondary complications such as pressure sores and flexural deformities. The ideal form of support would simply counteract the tensional support lost by the affected ligament or ligaments while retaining motion in all other planes. Hinged forms of orthotic devices are available and can be very successfully implemented. The primary problem with these types of devices is having enough braces to provide flexibility of sizing. Splints of this type are best used in a hospital environment because they often need to be reset more than once daily. A more flexible alternative is the use of pneumatic splints. They are a bit more troublesome in terms of inducing laxity but are very safe for use on outpatients because they are less likely to induce sores and are highly stable. The last alternative is tube casts or

splints applied over bandages. These again are problematic in their propensity to induce some laxity in the tendons, slow the intrinsic stiffening of the periarticular supporting structures, and induce sores. With any of these systems, judicious controlled exercise should be allowed for brief periods of time to speed the stabilization of the limbs. As stability improves, the degree and time of support is reduced, and the amount of work is increased.

Incomplete Ossification of the Cuboidal Bones

Incomplete ossification (IO) of the cuboidal bones is a sign of dysmaturity or prematurity. If the animal suffers from no concurrent deviations or ligamentous laxity, stall confinement to reduce trauma to the maturing bones should be sufficient therapy. This is rarely the case because most foals will have some amount of ligamentous instability. These foals generally require a more substantial degree of support, in the form of hinged splints, solid PVC splints, or tube casts. The goal is to protect the developing bones without weakening the tendons or ligaments any more than is necessary. Tube casts provide good support of the carpus and tarsus in all directions while maintaining some tension (loading) on the flexor tendons. These can be used in the hind limbs; however, pressure sores on the dorsal aspect of the proximal tibia, point of the calcaneus, and distal aspect of the metatarsus are common. When using tube casts in the hind limbs, owners should be informed that some foals will rupture the peroneus tertius. With continued rest most of these will heal uneventfully. External coaptation should be reduced and work increased gradually as the periarticular ligamentous structures strengthen and bones ossify.

Valgus and Varus Deviations

Therapy for correction of these angular deviations is directed at speeding growth on the concave side of the deviation or slowing growth on the convex side. The type of therapy is determined by the degree of angulation of the limb, site of the deviation, age of the animal, owner compliance, intended use of the animal, and clinician preference. Within the physiologic range, compression at the growth plate will speed growth-induced self-correction. For this reason, in many foals angular deformities will self-correct with nothing more than stall confinement and proper foot care. During this period of confinement trimming should be directed at removing hoof wall from the side of the foot on the convex side of the limb or extending the foot on the concave side with corrective shoes or epoxy extensions.

In instances in which owners seek a more rapid correction of angulation or the clinician considers the degree of deviation so severe that self-correction is not possible, surgical intervention is required. The indications for and effects of periosteal elevation are presently under great criticism. The basic principle behind the technique has always been the purported increased rate of growth of the metaphyseal bone on the concave side of a deviated limb with the net effect of straightening the limb. The procedure is often performed in conjunction with shoeing changes and confinement, which raises the question of exactly which part of the treatment benefits the animal.

In cases of severe deviations (>20 degrees) or in foals with minimal reserve growth potential in the affected

BOX 12.7-1**Surgical Technique for Periosteal Elevation**

1. Make a 5-mm incision along the long axis of the limb through the skin and periosteum.
2. Use a periosteal elevator to create an inverted T subcutaneous funnel extending 3 cm proximad, 2 cm cranial, and caudal to the skin incision.
3. Place a number-15 blade in a subcutaneous tunnel to transect the periosteum along the same path.
4. Use a periosteal elevator to conservatively elevate the transected margins of the periosteum.
5. Do not place sutures in the skin or subcutaneous tissues.
6. Apply nonadherent dressing and a firm pressure wrap to the skin.
7. Attach glue-on shoes while the foal is still under anesthesia.

bone, techniques designed to stop growth on the convex side of the limb are indicated. Ideally these techniques are used when the focus of deviation is in the metaphysis. This would be an instance whereby the actual point of deviation is corrected by the procedure. In many instances this is not the case, and we are creating a secondary deviation to create the illusion of a straight bony column. The most common bridging techniques are staples, screws and wires, or plates. These techniques carry an increased risk from the addition of implants. Although overwhelming infections that result in the destruction of the animal are very rare, infections and incisional complications that cause a less than optimal cosmetic appearance are not uncommon. Screws and plates are the preferred technique for correction of deviations in our practice. This technique utilizes implants that are readily available, can be performed through conservative incisions, rarely needs implant revision, and allows for easy removal of the implants. Details of surgical procedures can be found in Box 12.7-1.

In foals with severe angulations, in cases in which trauma has stopped growth, or in older animals with neared skeletal maturity, more aggressive techniques that involve osteotomies are required. These techniques require special skill in orthopedic surgical techniques and as such should be researched in a surgical text. The author's technique is described in Box 12.7-2.

COMPLICATIONS

Complications associated with management of angular limb deformities are fairly uncommon. The most common errors are associated with inappropriate use of splints and bandages. Without careful case supervision, bandage sores and induction of ligamentous laxity can become problematic. Simply monitoring the foal closely and frequently changing the bandage can generally avoid these problems. Complications associated with patients managed surgically usually fall into two classes—incisional infections and failure to correct the angulation. Incisional complications seem to be most common in foals with valgus angulations of the carpus. Interference at the medial surface of the carpus can occur with severe deviations that result in wound

BOX 12.7-2**Surgical Technique for Epiphyseal Bridging to Correct Angular Limb Deformity**

1. Identify the physis on radiographs taken during surgery and mark it with a 20-gauge needle.
2. Identify sites for screw placement.
3. Shift the skin cranial and make stab incisions at sites for epiphyseal and metaphyseal screws.
4. If possible, use a cannulated screw system to speed the procedure. (The guide pin maintains the stab incision over the site of screw placement.)
5. Drill holes, measure, and tap, if necessary. (Leave screw heads above the skin until the wire is placed.)
6. Using a periosteal elevator, make a subcutaneous tunnel between screws.
7. Pass a figure 8 loop of 16-gauge wire through the tunnel and over the proximal screw.
8. Tighten, cut, and fold the wire at the distal screw before tightening screws.
9. Close the skin incisions with a single intradermal layer of sutures.

trauma and dehiscence. For this reason this author believes as conservative a set of incisions as possible and being very diligent at placing the incisions as far caudad as possible is best. Once an incision has failed and an established infection is present around the implants, successful correction of the deformity is still possible. Daily wound care is generally enough to manage the local infection until the implants can be removed. If the clinician feels that the offending organism is inducing lameness or aggressive demineralization of the bone adjacent to the implants, antibiotics should be initiated. Attempts should be made to gain a culture of the infected site. In this author's hands, sterile preparation of the skin adjacent to the incision and suprapariosteal aspiration with a 19-gauge needle is the best technique. If dehiscence and exposure of the implants has occurred, most culture techniques are of limited value because they provide a sampling of the entire population of organisms in the wound's environment. In most of these cases diligent wound care will be enough to provide an environment conducive to correction of the angulation.

Failed correction of angular deformities is usually the result of poor patient selection or implant failure. Failures can occur due to delayed initiation of aggressive management or traumatic closure of physes in animals that should be well within the age frame for surgical correction. Implant failures usually involve the use of staples or screws and wires. In cases of severe angulation that have been managed with either of these techniques, radiographic reassessment is recommended for the affected limb at least every 3 to 4 weeks.

Supplemental Readings

- Auer JA: Angular limb deformities. In Auer JA, Stick JA (eds): *Equine Surgery*, 2nd edition, Philadelphia, WB Saunders, 1999.
- DeBowes RM: Carpal and tarsal bone anomalies. In White NA, Moore JN (eds): *Current Practice of Equine Surgery*, Philadelphia, JB Lippincott, 1990.

CHAPTER 12.8

Foal Pneumonia

W. DAVID WILSON

Davis, California

Pneumonia is the leading cause of morbidity and mortality in foals aged 1 to 6 months old and constitutes a major cause of economic loss to the equine industry. A crude incident morbidity of 6.1% was reported in a large prospective study of foal pneumonia on 167 farms in Texas, although the true incidence of infection of the lower airways of foals is most likely much higher; many cases of infection undoubtedly go unrecognized and resolve spontaneously. Indeed, careful weekly examination of Thoroughbred foals on farms in Ontario, Canada, demonstrated an average morbidity from bacterial infection of the distal respiratory tract of 82%. The impact of foal pneumonia on individual farms can be devastating. Mortality rates of 5% to 15% are common, but up to 80% of affected foals have died in some outbreaks, especially when *Rhodococcus equi* was the pathogen involved. The spectrum of clinical signs shown by affected foals is broad and reflects the severity and chronicity of the disease process, the degree of systemic sepsis, complicating environmental influences, and the pathogens involved. Most affected foals show tachypnea, abnormal respiratory character, nasal discharge, fever, and cough; however, the latter three signs are not consistent findings, even in severely affected foals.

During outbreaks, the disease process is often well advanced in the first foals to present, but additional foals are almost always infected but do not yet show prominent clinical signs. Identification of these foals, early recognition of new infections, and identification of patterns of spread and predisposing factors are very important if therapeutic and preventive measures are to be cost-effective and successful.

ETIOLOGY

The etiology of foal pneumonia is complex and involves the interaction of a number of predisposing factors with various microorganisms. The majority has bacterial involvement at the time of presentation and in most cases bacterial agents, particularly *Streptococcus equi* subspecies *zooepidemicus* (*S. zooepidemicus*) and *R. equi*, are primary pathogens. In other instances, viral agents such as influenza, equine herpesvirus-1 (EHV-1), EHV-4, EHV-2, rhinoviruses, adenoviruses, and possibly others are suspected to be predisposing factors; however, isolating the viral agent by the time the foal presents with signs of bacterial pneumonia is usually impossible. Viral agents compromise pulmonary defense by inducing ulceration of the respiratory epithelium, reducing mucociliary clearance, and impairing pulmonary alveolar macrophage function. In-

fluenza infection is uncommon in foals of well vaccinated mares, but primary viral pneumonia due to influenza A-equine-2 is recognized occasionally in young foals that have failed to acquire passive immunity and can prove fatal in severe cases. Foals born with congenital EHV-1 infection frequently have severe pneumonic lesions with or without pleural effusion, which is a condition that has a high mortality rate. Outbreaks of EHV-4 are common in sucklings and weanlings, with more severely affected foals showing pneumonic signs during the primary disease and after secondary bacterial infection.

Parasites may predispose to bacterial pneumonia by causing unthriftiness and, in the case of ascarid larvae, may cause pulmonary damage and a mild pneumonia directly during migration through the lung. This may induce eosinophilic bronchitis and pneumonitis, a condition also associated with *Dictyocaulus arnfieldi* infection in foals grazing with donkeys, asses, or mules. Most molds and fungi isolated from tracheobronchial aspirates of foals are thought to be environmental contaminants that do not contribute to the disease process. However, *Aspergillus* species, other fungal agents, and the funguslike organism *Pneumocystis carinii* have been isolated from foals with pneumonia on rare occasions, generally in association with immune deficiency states or prolonged antibiotic treatment. However, it has been suggested that *P. carinii* may play an etiologic role in acute respiratory distress syndrome in foals (see Chapter 12.9: "Bronchointerstitial Pneumonia and Acute Respiratory Distress").

Bacterial pneumonia is generally caused by opportunistic pathogens that are normal inhabitants of the equine upper respiratory tract or the gastrointestinal tract or are environmental contaminants. The frequency of isolation of each bacterial species varies between different geographic locations and polymicrobial infection is common. However, β -hemolytic *Streptococcus* species, especially *S. zooepidemicus*, are the most frequent isolates in all geographic locations, and *S. zooepidemicus* may spread between individuals as a transmissible pathogen. *Streptococcus equi* subspecies *equi* is not commonly isolated from the lungs of foals with pneumonia. *Rhodococcus equi*, a gram-positive pleomorphic rod (coccobacillus), occurs sporadically but is enzootic on some breeding farms (see Chapter 2.9: "*Rhodococcus equi* Infections"). Gram-negative nonenteric bacteria, including *Actinobacillus suis* species, other *Actinobacillus* species, *Pasteurella* species, and *Bordetella bronchiseptica* are also frequently isolated, either alone or in combination with *S. zooepidemicus* or other organisms. *Pseudomonas aeruginosa* and gram-negative enteric bacteria such as *Klebsiella pneumoniae*, *Escherichia coli*, and *Salmo-*

nella species are involved in some cases, particularly in younger foals in which infection was acquired during the neonatal period and are often associated with generalized sepsis. Other aerobic bacteria, such as *Staphylococcus* species, and anaerobic bacteria, are the etiologic agents in a small percentage of cases. However, anaerobic bacteria are isolated much less often from foals with bacterial pneumonia than from adult horses with pneumonia.

EPIDEMIOLOGY

The majority of foals with pneumonia are aged between 4 weeks and 6 months. The particularly high frequency of distal respiratory tract infection in foals in this age group has led some authors to suggest that a transient age-related immune deficiency exists. However, with the exception of a trough in the level of maternal antibody that occurs at a few months of age, standard procedures have failed to demonstrate immunologic defects in the vast majority of affected foals.

Of the interactive environmental and management factors that may predispose foals to the development of pneumonia, high ambient temperature appears to be important, especially when dry dusty conditions prevail. The demands for heat dissipation in hot climates may stress the respiratory system of foals, which appear to be less able than adults to tolerate extremes of temperature. In colder climates, chilling and overprotection from the cold—for instance, by reducing ventilation in a barn or excessive application of blankets—also appear to be detrimental. Overcrowding may stress foals and increases the concentration and transmission of pathogens both indoors and at pasture. Grass dies on overcrowded pastures, which then become dusty during dry weather if not irrigated. Dust irritates the respiratory tract and can compromise respiratory defense as well as acting as a fomite for potential pathogens, including *R. equi*. Indoors, warmth and humidity promote survival of pathogens and the stabilization and transmission of infective aerosols. Bedding may act as a source of dust and allergens and as a culture medium for certain bacteria and fungi. Poor stall drainage and sanitation, high temperature, and poor ventilation contribute to the build-up of noxious gases such as ammonia that compromise pulmonary defense. Many handling procedures, transportation, showing, and weaning can be stressful to foals. Weaning also results in the concentration of young susceptible animals and thus promotes disease spread. The common practice of transporting mares and foals to other farms for breeding and the mixing of visiting mares and foals or show horses with the resident foal crop also increases the likelihood of acquiring infection.

The epidemiology of *R. equi* infection has special features that contribute to the development of disease. The organism is a coprophilic soil inhabitant that is resistant to many disinfectants and tolerates desiccation and a wide range of soil pH. It survives for at least 12 months in soil that contains equine fecal material. Replication increases with increasing temperature, the optimal temperature for growth being 30° C. *R. equi* has been isolated from the gastrointestinal tract of horses and most other grazing herbivores and appears to multiply in the gastrointestinal tract

of foals up to 12 weeks of age. After passage in feces, *R. equi* proliferates rapidly in the aerobic environment of the fecal pat, resulting in 10,000-fold increases in numbers in a period of 2 weeks under optimal conditions of temperature, pH, and moisture. Citrate and propionate, the simple organic acid fermentation products of the large intestine, appear to be important growth factors. On farms on which infection is endemic, the organism has been found in highest numbers in soil in paddocks where horses have grazed and in dust in stables, holding pens, exercise areas, and aisles where infected foals have been kept. These areas appear to pose the greatest risk to young susceptible foals.

Mare feces and contaminated soil or dirt appear to be important sources of *R. equi* for colonization of the foal intestinal tract during the first few weeks of life. The coprophagic behavior of foals may be important in this regard. This colonization likely does not result in infection of the foal but rather in subsequent fecal shedding by foals and their dams, which, along with reduced moisture and increased environmental temperature, promotes multiplication of *R. equi* in fecal pats. Dry, windy conditions during the summer months promote dispersion of an increased number of organisms in the air, thus resulting in an increased aerosol challenge dose at a time when a large number of susceptible foals are present.

PATHOGENESIS

Most infections that cause foal pneumonia are thought to be acquired by inhalation of aerosolized or dustborne pathogens, but hematogenous seeding of the lung as a consequence of septicemia also occurs, especially in neonates. Aspiration pneumonia is encountered occasionally. Infectious agents suspended in aerosols or on dust particles tend to be deposited on the mucosa of the respiratory tract at the bronchiolar-alveolar junction. Colonization of the bronchiolar epithelium by opportunist bacteria occurs when pulmonary defense mechanisms are overwhelmed by massive challenge and when defenses are compromised by predisposing factors such as viral infection, transport stress, dust, or noxious gases. The resulting inflammatory response is characterized by the influx of neutrophils and other inflammatory cells into the airways and pulmonary parenchyma. Degranulation of neutrophils and other inflammatory cells causes damage to the airway epithelium and capillary endothelium, thus resulting in flooding of the terminal airways and alveoli with inflammatory cells, serum, cellular debris, and fibrin. This bronchopneumonic process is most prominent in the cranioventral portions of the lung—particularly the right lung—and causes reddish purple discoloration as involved areas become consolidated, heavy, and wet. These lesions interfere with gas exchange in affected areas, and if they are severe enough, the resulting ventilation/perfusion mismatch leads to hypoxemia and clinical manifestations of respiratory disease.

The basis for the pathogenicity of *R. equi*, a facultative intracellular parasite, is its ability to multiply within and destroy alveolar macrophages by inhibiting normal phagosome-lysosome fusion and perhaps by causing nonspecific degranulation of lysosomes. Destruction of macrophages and release of lysosomal products induces tissue damage

and provides both a constant source of infection and a stimulus for continued influx of macrophages and neutrophils. The result is persistence of an acute inflammatory response, even in chronic cases, with destruction of pulmonary parenchyma and formation of chronic pyogranulomatous mass lesions in the caudodorsal portion of the lung as well as in cranioventral areas, superimposed upon a prominent consolidating bronchopneumonia. This process appears to progress relatively slowly; thus signs may not become apparent until several weeks after infection. Incubation periods ranging from 10 days to more than 3 weeks have been noted in natural and experimental infections. Ingestion of large doses of the organism may lead to gastrointestinal lesions—particularly ulcerative enterocolitis and associated lymphadenitis—although the gastrointestinal tract is not thought to be a major portal of entry for pulmonary *R. equi* infections. Significant pyogranulomatous lesions may develop in the hilar, mediastinal, or mesenteric lymph nodes. Secondary bacteremia occurs occasionally and results in serious sequelae.

The polysaccharide capsule of *R. equi* appears to facilitate infection by helping the organism adhere to cells and may, along with mycolic acid-containing glycolipids, inhibit phagocytosis and killing by phagocytes. Other candidate virulence factors include cholesterol oxidase and choline phosphohydrolase exoenzymes (*equi* factors). Ingestion, phagosome-lysosome fusion, and killing of *R. equi* by macrophages and neutrophils is greatly enhanced by the presence of specific opsonic antibody and products of sensitized lymphocytes.

Expression of a family of closely related 15- to 17-kilodalton virulence-associated protein antigens (VapA and VapC through VapH), encoded by 80- to 90-kb plasmids, appears to be essential for virulence of *R. equi* isolates. This finding should prove helpful in developing approaches to immunoprophylaxis and helps explain why infection is endemic on some farms, sporadic on others, and not recognized on most despite the presence of a large number of horses that are shedding *R. equi* in their feces. Survey cultures of feces and tracheal wash samples in endemic herds indicate that the intestinal tract of the majority of foals becomes colonized with *R. equi* and that a substantial number of foals acquire subclinical pulmonary *R. equi* infection. These exposures appear to effectively immunize most foals. Antibodies against *R. equi* are common in the horse population and are passively transferred to foals in the colostrum. The decline in levels of passively acquired antibody results in an “antibody trough” at 8 to 10 weeks of age—or earlier if passive transfer is suboptimal—after which levels rise to those seen in adult horses by 6 months of age. It has been thought that those foals that develop *R. equi* pneumonia do so because they receive an overwhelming challenge at a time when passive humoral protection is waning and before the foal has mounted a specific immune response. However, recent evidence suggests that many foals become infected during the first few weeks of life.

CLINICAL PRESENTATION

The history and clinical presentation of foals with infection of the lower respiratory tract varies considerably. The

spectrum ranges from an otherwise normal-appearing foal with intermittent coughing and mild mucopurulent nasal discharge to one with a high fever, severe depression, anorexia, profuse purulent nasal discharge, severe respiratory distress, and cyanosis. Tachypnea and altered respiratory character are typical features, even in mildly affected foals, and are best assessed at rest with minimal restraint during the cool part of the day. Respiratory rates greater than 40 per minute in an older foal or weanling at rest are considered abnormal under most circumstances, and resting rates greater than 30 per minute during the cool early morning hours are cause for concern and warrant further evaluation of the foal. Increased intercostal effort, often characterized by asynchronous rib excursion (rippling of the rib cage), is a subtle but frequent early sign. More severely affected foals also show nostril flaring, increased abdominal effort, or frank abdominal breathing with minimal costal excursion. These foals are exercise-intolerant; show an anxious expression; are reluctant to lie down, nurse, or move; and may develop signs of severe respiratory distress, cyanosis, and disorientation if stressed or forced to exercise.

Coughing is an important clinical sign, but it is not invariably present, particularly in foals with *R. equi* pneumonia. In early cases, coughing is generally most obvious in the morning when the foal is disturbed or restrained after lying down, or after brief exercise. The nature of the cough varies from intermittent, moist, and shallow to paroxysmal, deep, and hacking. Almost all affected foals cough when a rebreathing bag is applied, whereas normal foals rarely do so. A bilateral mucopurulent nasal discharge that varies in amount from profuse to scant and intermittent is a common finding. In some foals the only evidence of a nasal discharge is dry crusting at the external nares or dried exudate on the dorsal aspect of the front cannon area deposited when the foal wipes its nose. Exudate from the lower airways may be swallowed and not appear as a nasal discharge. Some foals, including a substantial proportion of those with *R. equi* pneumonia, do not have a nasal discharge. Fever—usually in the range of 38.8° to 40.0° C (102°–104° F) but sometimes in excess of 40.5° C (105° F)—is a common finding in foals with pneumonia. However, the rectal temperature is frequently normal in foals with infection of the distal respiratory tract that lack significant parenchymal lesions. Demeanor and appetite are highly variable and do not necessarily reflect the severity of underlying pulmonary pathology. Most affected foals are well grown and in good flesh, but weight loss and stunting may become apparent with chronicity.

Most clinical cases of *R. equi* pneumonia represent the chronic form of the disease; a smaller percentage experiences a more fulminant subacute form. However, respiratory signs are often of acute onset and reflect the insidious progression of the disease process until sufficient lung is damaged to cause respiratory failure. In addition, the subtle early signs of disease are often missed or ignored by horsemen, thereby allowing the condition to progress to a more advanced stage before veterinary help is sought. Although recognizing the etiologic cause of foal pneumonia based on clinical signs alone is impossible, the clinical presentation and clinical pathology findings in foals with

R. equi infection present some features that increase the index of suspicion. These include lack of nasal discharge, presence of fever, markedly delayed recovery from application of a rebreathing bag, peripheral neutrophilia and marked hyperfibrinogenemia, and a relatively lower percentage of neutrophils in bronchial lavage fluid than is usually encountered with other bacterial agents.

Auscultation, both at rest and after application of a rebreathing bag, if not precluded by severe respiratory distress, is very helpful in defining the presence, extent, and nature of lung involvement when findings are interpreted in the context of other signs, such as respiratory rate and character. The lung sounds in foals with distal respiratory tract infection vary considerably, and sounds referred from the upper airway can confuse auscultation findings. Foals with a large amount of tenacious exudate in the trachea often have an audible and palpable tracheal rattle. Mildly affected foals have increased audibility and harshness of expiratory and inspiratory bronchovesicular sounds and increased tracheal sounds that reflect the presence of exudate. Occasional inspiratory and expiratory wheezes and crackles are usually audible over involved areas, which are most often located cranioventrally. In many early cases, adventitious sounds are audible only when a rebreathing bag is used. In more severely affected foals, increased tracheal and bronchovesicular sounds are accompanied by fine and coarse crackles and widespread polyphonic wheezes. In some cases wheezes are audible at the nostrils, and the inciting turbulence is also palpable on the chest wall. Lung sounds are diminished over areas of severe consolidation, extensive abscess formation, or pleural effusion. These areas may also show reduced resonance on chest percussion; however, pleural effusion is not commonly present in foals with pneumonia.

DIAGNOSIS

Diagnostic evaluation should be directed at the entire herd as well as at further assessment of sick foals. Evaluation of individual foals should establish whether infection of the distal respiratory tract is present and should determine the etiology and severity of pulmonary involvement so that appropriate therapeutic measures can be instituted and an accurate prognosis rendered. Important features of the history in affected foals include age; duration and progression of signs; response to treatment; previous cases in the herd including agents isolated, antimicrobial susceptibility, and response to treatment; herd history of viral respiratory disease and vaccination; season; general herd management; parasite control; movement of horses on and off the farm; and the presence of other clinical signs such as diarrhea or lymphadenopathy in the affected foal or herd mates. In addition to examination of the respiratory system, a general physical examination should be performed with particular attention to hydration status, mucous membrane color and capillary refill, the umbilicus, joints, and the lymph nodes of the head and neck. *R. equi* infections occasionally cause diarrhea, and up to 30% of foals with *R. equi* pneumonia also show a chronic, active, nonseptic (likely immune-mediated) synovitis characterized by neutrophilia in synovial fluid and joint distention with minimal or absent lameness. Panophthalmitis, septic arthritis,

physitis, and osteomyelitis—including vertebral body osteomyelitis—have also been encountered in foals with *R. equi* infection.

The need for ancillary diagnostic procedures is determined by the herd history, the number and value of foals affected and at risk, the time of year relative to the foaling season, management practices, available facilities, severity and duration of clinical signs, treatments used, and response. In foals with pneumonia, measurement of complete blood count (CBC), plasma protein, and fibrinogen concentration commonly shows evidence of a moderate to marked inflammatory response characterized by leukocytosis with neutrophilia with or without a left shift and an elevated fibrinogen concentration. However, a strong correlation seems to exist between the severity of clinical signs and the magnitude of CBC changes. Indeed, many foals with infection of the distal respiratory tract have a normal leukocyte count. Sequential measurement of plasma fibrinogen concentration often provides a useful means of monitoring response to treatment and helps guide the decision to discontinue treatment. In general, antibiotic treatment should not be discontinued until plasma fibrinogen concentration has returned to the normal range (≤ 400 mg/dl). A CBC test result also allows evaluation of hydration and preliminary screening of the immune system. If the lymphocyte count is consistently low ($<1000/\mu\text{l}$), immune function should be evaluated more thoroughly, particularly in Arabian foals. Similarly, the adequacy of colostral antibody transfer should be determined in foals younger than 1 month of age. The thrombocytosis noted consistently in *R. equi* cases by workers in Ireland has not been reported by workers elsewhere. This finding most likely reflects differences between laboratories in the method used to quantify equine platelets rather than being a unique feature of *R. equi* infections in Ireland.

Ultrasonographic evaluation of the chest with a 5.0- to 7.5-MHz sector or linear probe provides a rapid and sensitive means of detecting pleural effusion and pulmonary consolidation or abscesses in the peripheral lung; however, the procedure does not detect deep pulmonary lesions surrounded by normally aerated lung. Although pleural effusion is rare in foals, ultrasound examination often reveals pleural thickening and roughening ("comet tails") in foals with pneumonia.

Tracheobronchial aspiration with cytologic examination and aerobic and anaerobic bacteriologic culture with susceptibility testing of aspirated material are the most definitive diagnostic procedures available. The results of bacteriologic culture should be interpreted in the context of the results of cytologic evaluation that shows evidence of inflammation that results from infection. Positive culture results—including isolation of *R. equi*—in the absence of cytologic evidence of inflammation occurs on occasion and constitutes a false positive culture result. Because the number as well as species of bacteria may be important, quantification of growth should be attempted. A polymerase chain reaction (PCR) test for *R. equi* is now available and is used by some as an alternative to or adjunct to culture. In the field setting, performing transtracheal washes on all foals with pneumonia is not always practical or desirable. On breeding farms where multiple cases are likely to occur—especially if *R. equi* has been a problem in

previous years—a reasonable approach is to perform tracheal washes on the first few affected foals in an outbreak to establish which organisms are involved and their antibiotic susceptibility patterns. Thereafter, washes should be performed on any foal that is not responding to the chosen treatment, foals with atypical signs, and foals with other evidence such as radiographic changes of *R. equi* pneumonia. Depending on the chronicity of the condition, a period of at least 3 days is generally needed to assess the response to initial treatment. Whenever possible, antibiotic treatment should be discontinued at least 24 hours before performing tracheal washes on foals that are nonresponsive to initial treatment. The recent introduction of aspiration catheters that can be passed through the biopsy port of an endoscope has facilitated collection of appropriate diagnostic samples and provides an alternative to the transtracheal technique. Similarly, the use of a guarded bronchoscope fitted with a clear sterile cellulose acetate sheath provides an excellent method for collection of uncontaminated samples from the lower airways. In addition, endoscopic examination is helpful in ruling out predisposing or concurrent upper airway abnormalities such as guttural pouch empyema and in documenting bronchial erythema, exudate, and edema, all of which indicate inflammation of the distal respiratory tract. Nasopharyngeal swabbing is useful for diagnosing acute viral respiratory tract infection and strangles but not bacterial infection of the lower airways.

On cytologic evaluation of smears of the cell pellet from tracheobronchial aspirates, particular attention should be given to the types and numbers of cells, their state of degeneration, and the presence, number, location (intracellular or extracellular), morphology, and staining characteristics of bacteria. *S. zooepidemicus* is often recognizable on direct smears by the presence of a prominent halo that represents its nonstaining capsule. Accurate cytologic evaluation aids diagnosis and assists in selection of initial antibacterial treatment before final culture results are available. Bacteria, particularly gram-negatives, are often seen on a direct smear but fail to grow in culture in foals that have already been treated with antibiotics. In *R. equi* infections, false-negative culture results have been noted, but in at least 60% of cases, cytologic examination of tracheobronchial aspirates demonstrates the characteristic pleomorphic gram-positive coccobacilli located intracellularly and extracellularly. Special staining techniques may be necessary to identify unusual pathogens such as *Pneumocystis carinii*.

Radiography is a useful diagnostic technique, especially in more severe cases in which consolidation or abscessation is suspected or in which *R. equi* is the suspected or confirmed pathogen. The procedure is also helpful in evaluating the response to treatment. The presence of air bronchograms in the cranioventral lung field, increase in interstitial density, variously sized “cotton-ball” or cavity densities in the lung field, and hilar lymphadenopathy are typical radiographic features of *R. equi* pneumonia. Thoracic radiography is particularly useful in the evaluation of pneumonia in neonatal foals because clinical and auscultation findings in this age group often do not correlate well with the degree of pulmonary consolidation present. The use of rare-earth screens and air-gap techniques makes

it possible to take chest radiographs on smaller foals using some portable radiograph machines (see Table 1 in *Current Therapy in Equine Medicine*, third edition, p. 470).

Currently, no serologic tests reliably detect early infection with the bacterial species commonly associated with foal pneumonia. Sensitive enzyme-linked immunosorbent assay (ELISA) tests, which detect antibodies directed against cell wall components of *R. equi*, are useful for epidemiologic investigation and herd monitoring but are not useful adjuncts to diagnosis. The agar gel diffusion test, synergistic hemolysin inhibition test, and immunodiffusion test, which detect antibodies directed against the cholesterol oxidase coenzyme (“equi factor”) produced by actively replicating *R. equi* organisms, have been advocated as being useful for the early diagnosis of *R. equi* infections. However, both false-negative and false-positive results have been observed, and a lag period of several weeks generally occurs between infection and detection of antibodies with these tests. In addition, an ELISA test has been shown experimentally to be useful in the diagnosis of infection, but the antigens used for the test remain to be defined.

Blood gas analysis is very useful for monitoring the oxygenation and acid-base status during therapy of affected foals showing signs of marked respiratory distress or cyanosis. Culture of blood frequently yields bacterial growth in neonatal foals with pneumonia, and *R. equi* may be isolated from blood of affected foals showing signs of systemic infection. A bronchodilator response test with atropine or β_2 -adrenergic drugs such as clenbuterol or albuterol may help in the evaluation of those foals that continue to show signs of obstructive lung disease after resolution of the bacterial pneumonia. Other diagnostic procedures that are useful in selected situations include fecal flotation for parasites, bronchoalveolar lavage, virus isolation, serology for respiratory viruses, immune function tests, and thoracocentesis. A thorough necropsy examination—including culture and susceptibility testing of pneumonic lesions, abscesses, and exudates—should be performed on any foal that dies.

After completing the diagnostic evaluation and initiating treatment on the first foal(s) presented for examination, herdmates should be screened for evidence of infection, and a protocol should be established to facilitate early detection of new infections. On farms on which foals are halter-trained and handled regularly, the best approach is to perform physical examinations on all foals at risk and to perform appropriate diagnostic procedures on those with signs suggestive of infection. Thereafter, careful observation—daily or twice daily recording of rectal temperature and regular weighing—facilitate early detection of new infections. In addition, performance of complete physical examinations, including pulmonary auscultation twice weekly, has proven successful in promoting early diagnosis of *R. equi* infection and in preventing mortality. If economics permit, routine screening for complete blood count, fibrinogen concentration, and serology for viral infections and *R. equi* may further improve diagnostic sensitivity for early bacterial infection and the identification of predisposing viral agents.

On farms on which foals are unaccustomed to being handled, assembly and restraint for examination may prove unnecessarily stressful to the foals, may distort the

findings of clinical and laboratory examinations, and may actually facilitate transmission of infectious agents. A useful approach under these circumstances is to observe all foals at rest in their paddocks during the cool early morning hours before they are disturbed by feeding and other management activities. Foals that show evidence of listlessness, tachypnea, altered respiratory character, nasal discharge, depression, poor body condition, excessively rough hair coat, repeated coughing when disturbed, or other signs of disease are selected for a more complete physical examination and appropriate further diagnostic evaluation.

TREATMENT

An integrated approach is required to not only destroy the causal organisms with specific antimicrobial therapy but also improve respiratory function, minimize stress, and maximize patient comfort and environmental quality. Restricting exercise is important initially in more severe cases to reduce ventilatory demands. In milder cases and in those that are improving with treatment, limited exercise may be helpful in promoting expectoration. Confinement in a cool, clean, dust- and odor-free, well-ventilated enclosure is indicated to minimize activity and exposure to the elements. Screened doors and wall panels promote ventilation at foal level. Sprinklers can be used to control dust in paddocks and pastures, and feeders should be moved to a grassy area if possible. Other dusty areas such as aisles and stalls in barns should be cleaned and watered down regularly during hot dry periods. Barns with poorly insulated roofs can be cooled with roof-mounted water sprinklers on hot days. Confinement in an air-conditioned stall may be necessary for foals with marked respiratory distress.

Antibacterial Treatment

Systemic antibacterial treatment should be based on the nature and severity of clinical signs, results of culture and susceptibility testing of tracheobronchial aspirates, experience within the herd and locale, and the properties of the chosen drugs that determine their distribution to inflamed lung tissue in therapeutic concentrations (see Table 2 in *Current Therapy in Equine Medicine*, third edition, p 471).

In addition, the required route and frequency of drug administration, side effects, toxicity, and relative cost of therapy are important considerations. Initiation of antibacterial treatment before the results of culture and susceptibility testing are known is generally necessary, and in many instances treatment proceeds without samples for culture being obtained. Because β -hemolytic *Streptococcus* species are the most common bacteria isolated from pneumonic foals older than 30 days of age, penicillin G is a logical choice for initial treatment in circumstances when *R. equi* has not previously been a problem. This drug also shows activity against many isolates of gram-negative nonenteric organisms such as *Actinobacillus suis* and *Pasteurella* species. When involvement of penicillin-resistant gram-negative organisms is suspected or confirmed, an effective antibiotic that is compatible with penicillin should be included in the regimen. Aminoglycoside antibiotics

such as gentamicin (7 mg/kg IV or IM q24h) or amikacin (21 mg/kg IV or IM q24h) are logical choices, but these agents should not be used alone because of their poor activity against β -hemolytic *Streptococcus* species. Trimethoprim/sulfonamide combinations (TMS) have a broad spectrum of activity, which includes many of the causal agents of foal pneumonia and can be administered by the oral route (24-30 mg/kg of combination q12h) to initiate treatment. Trimethoprim/sulfonamide can be used alone or with penicillin G when TMS-susceptible, penicillin-resistant bacteria are present in mixed infections with gram-positive organisms. Ceftiofur, a third-generation cephalosporin antibiotic, has a broad spectrum of activity that includes most of the etiologic agents of foal pneumonia, except *R. equi*. Doses of 2.2 to 5.0 mg/kg IM every 12 hours are recommended depending on the minimum inhibitory concentration (MIC) of the causal organism. Antibiotic treatment should be continued for 5 to 7 days after the foal is clinically normal; otherwise a high rate of relapse is encountered. If the foal does not show clinical improvement within 3 to 5 days after initiation of treatment, the therapeutic regimen should be reevaluated, including a repeated tracheal wash. Chronic cases generally respond more slowly than do acute cases.

The treatment of *R. equi* pneumonia requires special consideration. *R. equi* is susceptible *in vitro* to a wide range of antibiotics—including amikacin, gentamicin, neomycin, chloramphenicol, trimethoprim/sulfonamide, erythromycin, and rifampin. However, the dramatic increase in recovery rates since the introduction of oral treatment with erythromycin/rifampin makes this the therapeutic approach of choice. These lipid-soluble agents show synergistic activity *in vitro*; both effectively penetrate cell membranes to achieve therapeutic concentrations in the lung, bronchial secretions, and within phagocytes where the organism multiplies; and both appear to be active in the environment of pyogranulomas, thus sterilizing them. In addition, both drugs show excellent activity against *Streptococcus* species and acceptable activity against most *Actinobacillus* species, organisms that are often isolated along with *R. equi*. Although the vast majority of *R. equi* isolates are susceptible to erythromycin and rifampin, resistant strains have been encountered.

It is recommended that erythromycin (20 to 25 mg/kg PO q8h), as the acid-stable estolate ester or as microencapsulated erythromycin base, be used with rifampin (5 to 7.5 mg/kg PO q12h) to initiate therapy. Absorption of erythromycin estolate is superior to that of other dosage forms of erythromycin, thus suggesting that a dosing regimen of every 12 hours may be appropriate after a positive response to treatment every 8 hours has been observed. Similarly, use of a lower dose of rifampin (2.5 to 5 mg/kg PO q12h) after a positive response has been achieved with the higher dose has proven effective and reduces treatment costs. Rifampin causes reddish discoloration of urine, and the erythromycin-rifampin combination often causes the fecal consistency to soften. The occurrence of the latter side effect does not necessitate discontinuation of treatment, but these foals should be monitored carefully because some will develop depression, severe diarrhea, dehydration, and electrolyte loss, thus necessitating cessation of antibiotic treatment and initiation of intensive fluid and electrolyte

therapy. Similar side effects have been noted on occasion when rifampin is used in combination with penicillin G or TMS. Erythromycin and rifampin may give rise to transient signs of partial anorexia, mild colic, and bruxism that usually resolve if the horse's mouth is washed out within an hour after administering the dose or on temporary cessation (one to two doses) of treatment.

Oral erythromycin alone has been used successfully to treat *R. equi* pneumonia, but comparison of efficacy with the erythromycin/rifampin regimen awaits confirmation. In addition, idiosyncratic reactions characterized by hyperthermia, tachypnea, or overt respiratory distress have been seen in foals being treated with erythromycin during hot weather. Diarrhea has been observed occasionally in the dams of nursing foals when the foals are being treated with oral erythromycin, presumably because coprophagic behavior leads to ingestion of sufficient active erythromycin to disrupt the normal gastrointestinal flora of the mare.

Although erythromycin and rifampin are the drugs of choice for treating *R. equi* infection, it may be necessary to use other drugs or combinations for individual foals. Parenteral treatment with gentamicin (7 mg/kg IV or IM q24h) in combination with penicillin G or ampicillin has proven to be therapeutically effective in some cases, although the use of gentamicin along with oral rifampin appears to be a more effective approach for treating foals that experience adverse side effects such as hyperthermia and respiratory distress that preclude the use of erythromycin.

Azithromycin and clarithromycin are macrolide antibiotics that show enhanced absorption from the GI tract, longer elimination half-life, more persistent tissue concentration, and broader antimicrobial spectrum than erythromycin in humans. Azithromycin reaches concentrations in macrophages that are 80 to 100 times higher than the peak concentration achieved in serum. Absorption of azithromycin in foals is superior to that of erythromycin, such that an oral dose of 10 mg/kg every 24 hours for 5 days followed by the same dose every other day until lesions resolve (usually 1 to 3 weeks) has proven effective for the treatment of *R. equi* pneumonia and pneumonia caused by other susceptible pathogens. Limited experience suggests that efficacy is improved when rifampin is used in combination with azithromycin. Elevation in serum concentrations of liver enzymes without clinical evidence of liver disease has been observed in some foals treated with azithromycin. Rarely does this finding necessitate discontinuing therapy, but skipping one or more doses or widening the dosage interval may be indicated until enzyme concentrations return toward the normal range. Foals may develop diarrhea while being treated with azithromycin and rifampin, but severe colitis appears to be a less common side effect than with some oral erythromycin formulations. The recommended dose of clarithromycin is 7.5 mg/kg by mouth every 12 hours, pending results of clinical studies.

The severe consolidating pulmonary lesions that characterize *R. equi* infection necessitate early recognition and prolonged treatment to achieve a satisfactory outcome. Resolution of clinical signs, normalization of plasma fibrinogen concentration, white blood cell (WBC) count and thrombocyte count, and radiographic resolution of

lesions are used to guide the duration of therapy, which generally ranges between 3 and 12 weeks. Relapses may occur if treatment is prematurely discontinued. A positive clinical response within 7 days suggests a favorable prognosis. Recovery rates exceeding 80% have been reported for referred, presumably serious, *R. equi* cases.

Clearing Secretions

Maintenance of adequate hydration is important to promote mucociliary clearance and expectoration by reducing the viscosity of tenacious bronchial secretions. This can usually be accomplished by the provision of clean water, but parenteral therapy with polyionic electrolyte solutions may be indicated in some cases. Intravenous fluid therapy should be monitored closely because pneumonia predisposes foals to the development of pulmonary edema. Expectorants such as iodides, guaifenesin, volatile oils, and sulfonamides are often beneficial by helping mobilize respiratory secretions. Mucolytics, such as bromhexine hydrochloride or a newer derivative (Sputolysin, Boehringer Ingelheim, Bracknell, England) can also be beneficial in cases with large amounts of mucus in the airways. Cough suppressants are generally contraindicated but may be needed in the occasional foal that becomes exhausted by paroxysmal coughing.

Nebulization is often helpful in foals with tenacious secretions or a nonproductive cough but is contraindicated in foals with voluminous moist secretions, and the procedure may prove too stressful to some foals. The major functions of nebulization are to humidify and liquefy secretions, relieve bronchospasm, decrease mucosal edema, and kill bacteria. Ultrasonic nebulizers that disperse droplets less than 5 μm in diameter should be used. Saline alone is useful for liquefying tenacious secretions, and saline is also the usual choice as a carrier solution for other agents such as bronchodilators, mucolytics, and antibiotics. The aerosol is delivered through a loose-fitting mask, such as a gallon or half-gallon plastic jug, with 15- to 30-minute exposures at 6- to 12-hour intervals. The formula in Box 12.8-1 has been reported to be a useful nebulizing formula for foals with pneumonia caused by *R. equi* or gram-negative organisms.

Another nebulizing formula reported to be successful is 10 ml N-acetylcysteine (20%), 10 ml isoetharine HCl inhalation (1%), 10 ml gentamicin sulfate (50 mg/ml), and 50 ml normal saline.

Maintaining Gas Exchange

Oxygen therapy with humidified oxygen (6-10 L/minute) delivered by nasal insufflation, via a loose-fitting mask or—in severely hypoxemic foals—via percutaneous transtracheal administration is indicated in foals that show severe respiratory distress and persistent hypoxemia or cyanosis. Nonsteroidal antiinflammatory drugs (NSAIDs) such as phenylbutazone, flunixin meglumine, or dipyrone may be of value in limiting the pulmonary inflammatory reaction as well as in reducing fever and improving attitude and appetite in febrile, depressed, anorectic foals. However, these drugs may negate the value of temperature in monitoring the effectiveness of therapy, may predispose to gastric ul-

BOX 12.8-1**Nebulizing Formula for Foals with Pneumonia Caused by *Rhodococcus equi* or Gram-Negative Organisms**

Carrier solution: half-strength saline (180 ml)
 Mucolytic: N-acetylcysteine 20% (5 to 10 ml)
 Bronchodilator isoproterenol (2 ml) or isoetharine HCl inhalation, 1% (1 ml)
 Antibiotic: gentamicin sulfate (150 mg) or kanamycin sulfate (400 mg)

ceration, and can be nephrotoxic in hypovolemic foals. These cases should be monitored carefully, and the NSAID dose should be reduced or discontinued when the foal's attitude and appetite improve.

The use of bronchodilator drugs in treating foal pneumonia is controversial, but this author has found that some foals judged to have widespread bronchoconstriction on the basis of clinical findings or the results of bronchodilator response tests may benefit considerably from bronchodilator therapy. Clenbuterol (0.8-3.2 µg/kg PO q12h), aminophylline (5-10 mg/kg PO q12h) or albuterol by inhalation have proven beneficial in selected patients, particularly those that have abnormal respiratory character (increased expiratory effort) and adventitious lung sounds after the bacterial component has been eliminated with antibiotic therapy. Culture-negative cases of this type appear to be suffering from hyperreactive small airway disease with excess mucus secretion similar to that seen in adult horses with chronic obstructive pulmonary disease. Aminophylline treatment should be short-term and monitored carefully because clinical signs may deteriorate in some foals because of cardiotoxicity and increased ventilation/perfusion mismatch. In addition, the elimination of aminophylline may be delayed by erythromycin; thus blood levels may be increased and toxicity potentiated. If the response to environmental improvement (minimum-dust management) and bronchodilator treatment is poor, short-term low-dose treatment with corticosteroids, such as dexamethasone (0.02-0.05 mg/kg q24h for 4-7 days), may be necessary to break the inflammatory, mucus-secreting cycle and promote resolution in foals with hyperreactive airway disease.

Immunotherapy

Supplementation or augmentation of the immune response may be beneficial in selected patients. Plasma transfusion is indicated in young foals with pneumonia and partial or complete failure of passive transfer of colostral antibody and may benefit foals that are hypoproteinemic for other reasons. Specific hyperimmune *R. equi* plasma has been shown to effectively prevent *R. equi* pneumonia after natural and experimental challenge, but the value of hyperimmune plasma in treating established *R. equi* infection appears to be more limited. Immunomodulatory drugs such as mycobacterial cell wall extract and extracts of *Propionibacterium acnes* are nonspe-

cific stimulators of the immune response and have gained widespread use in recent years as adjuncts to conventional treatment of respiratory tract infection, particularly chronic foal pneumonia. Levamisole, a modulator of T cell function, has also been recommended for use in foals with chronic nonresponsive pneumonia. The use of immunomodulatory drugs may increase as the rationale for their inclusion in therapeutic regimens becomes supported by controlled independent studies to document their efficacy. The majority of foals with bacterial pneumonia, including those with serious *R. equi* infection, survive and appear to maintain the potential to become successful performance horses.

PREVENTION

The cornerstone of prevention is good herd management. This involves good hygiene and sanitation, maximizing environmental quality, avoiding overgrazing and overcrowding, reducing dust, employing strict parasite control, vaccinating to prevent viral respiratory infection, enforcing rest if viral respiratory infection does occur, maintaining fixed herd groups, separating resident horses from visiting horses, and isolating new arrivals and clinically ill horses. Farms and feeding and watering arrangements should be designed so that foals are dispersed rather than concentrated, and the size of mare-foal bands should be restricted to 10 pairs or fewer. Foaling management is also very important—particularly the booster vaccination of mares against respiratory pathogens before foaling, ensuring adequate early colostral intake by foals, paying attention to the foal's umbilicus at foaling, and avoiding transportation and mixing of young foals from different sources. Provision of adequate shade is important for horses pastured in hot sunny climates. Extreme care must also be taken when transporting foals, especially those with respiratory disease, during the summer months because the interior of horse trailers can become extremely hot, particularly when the trailer is parked. As noted previously, foals should be observed closely for signs of respiratory disease because early diagnosis of pneumonia is important if treatment is to be cost-effective and successful.

Routine preventive measures outlined for the control of foal pneumonia, although helpful, have not prevented serious outbreaks of *R. equi* on individual breeding farms. The following three specific preventive measures should be considered when designing approaches to prevention of *R. equi* pneumonia:

1. Decreasing the size of infective challenge
2. Promoting early recognition of the disease
3. Passive immunization to improve resistance.

Considering the coprophilic nature of *R. equi* and the progressive amplification of *R. equi* numbers during the summer months in paddocks, holding pens, barn aisles, and walkways, strict attention to removal of feces from these areas, the use of clean paddocks for foals, promotion of grass growth in paddocks, and reduction of dusty or sandy conditions in the environment of foals are indicated to reduce the level of challenge. Despite the poor results achieved by vaccinating foals or their dams (prefoaling) with *R. equi* bacterins, recent evidence indicates that some factors, regardless

of whether they are antibody-specific, present in hyperimmune plasma may be important in conferring resistance to infection. A program in which hyperimmune plasma (1 L) is administered to foals aged 2 to 7 days and, if necessary, repeated at 3 to 4 weeks of age has greatly reduced the incidence of *R. equi* pneumonia on problem farms. Two commercially available hyperimmune plasma products (Polymune R, Veterinary Dynamics, Inc., Templeton, Calif.; *Rhodococcus equi* antibody, Lake Immunogenics, Inc., Ontario, N.Y.) have been granted conditional licenses by the United States Department of Agriculture (USDA) and are recommended for administration to individual foals or to the entire foal crop on premises with endemic *R. equi* when the expense of this approach is outweighed by the costs associated with treatment and mortality.

Supplemental Readings

- Cohen ND: Causes of and farm management factors associated with disease and death in foals. *J Am Vet Med Assoc* 1994; 204:1644-1651.
- Giguère S: *Rhodococcus equi* pneumonia. Proceedings of the 47th Annual Convention of the American Association of Equine Practitioners, pp 456-467, 2001.
- Hillidge CJ: Use of erythromycin-rifampin combination in treatment of *Rhodococcus equi* pneumonia. *Vet Microbiol* 1987; 14:337-342.
- Hoffman AM, Viel L, Juniper E et al: Clinical and endoscopic study to estimate the incidence of distal respiratory tract infection in Thoroughbred foals on Ontario breeding farms. *Am J Vet Res* 1993; 54:1602-1607.
- Hoffman AM, Viel L, Prescott JF et al: Association of microbiologic flora with clinical endoscopic, and pulmonary cytologic findings in foals with distal respiratory tract infection. *Am J Vet Res* 1993; 54:1615-1622.
- Madigan JE, Hietala S, Mueller N: Protection against naturally acquired *Rhodococcus equi* pneumonia in foals by administration of hyperimmune plasma. *J Reprod Fertil* 1991; 44[Suppl]:S71-S78.
- Martens RJ, Ruoff WW, Renshaw HW: Foal pneumonia: a practical approach to diagnosis and therapy. *Comp Cont Educ Pract Vet* 1982; 9:S361-S375.
- Prescott JF, Hoffman AM: *Rhodococcus equi*. *Vet Clin North Am Equine Pract* 1993; 9:375-384.
- Sellon DC: Investigating outbreaks of respiratory disease in older foals. Proceedings of the 47th Annual Convention of the American Association of Equine Practitioners, pp 447-455, 2001.
- Sweeney CR, Sweeney RW, Divers TJ: *Rhodococcus equi* pneumonia in 48 foals: response to antimicrobial therapy. *Vet Microbiol* 1987; 14:329-336.

CHAPTER 12.9

Bronchointerstitial Pneumonia and Acute Respiratory Distress

W. DAVID WILSON

Davis, California

JEFFREY LAKRITZ

Columbia, Missouri

A sporadic, rapidly progressive, high-mortality, acute respiratory distress syndrome (ARDS) has been described in foals aged between 1 week and 8 months. The syndrome appears to be distinct from the acute respiratory distress syndrome seen in neonatal foals and has been encountered in Canada, the northeastern United States, Florida, Kentucky, Oklahoma, Kansas, California, Britain, Denmark, and France. It probably also occurs elsewhere.

ETIOPATHOGENESIS

This syndrome likely does not have a single etiology but rather represents the common reaction of the lung to a number of different insults, the precise nature of which remains to be determined. A viral etiology has been pro-

posed based on the sporadic nature of the disease, the age incidence, and the histologic lesions, which include multinucleate syncytial cells similar to those seen with bovine respiratory syncytial virus (BRSV) infection in cattle. Although viruses such as influenza virus and equine adenovirus are capable of causing diffuse alveolar damage and although certain strains of equine influenza A-equine-2 virus have been reported to induce severe fatal pneumonitis and respiratory distress in foals, viral agents do not appear to be involved in the majority of cases of ARDS.

Pneumocystis carinii has been implicated as a potential cause of ARDS in foals, based on the identification of this organism in the lungs of a number of fatally affected foals in Britain, the northeastern United States, Canada, Florida, and Japan. This parasite, a unicellular

of whether they are antibody-specific, present in hyperimmune plasma may be important in conferring resistance to infection. A program in which hyperimmune plasma (1 L) is administered to foals aged 2 to 7 days and, if necessary, repeated at 3 to 4 weeks of age has greatly reduced the incidence of *R. equi* pneumonia on problem farms. Two commercially available hyperimmune plasma products (Polymune R, Veterinary Dynamics, Inc., Templeton, Calif.; *Rhodococcus equi* antibody, Lake Immunogenics, Inc., Ontario, N.Y.) have been granted conditional licenses by the United States Department of Agriculture (USDA) and are recommended for administration to individual foals or to the entire foal crop on premises with endemic *R. equi* when the expense of this approach is outweighed by the costs associated with treatment and mortality.

Supplemental Readings

- Cohen ND: Causes of and farm management factors associated with disease and death in foals. *J Am Vet Med Assoc* 1994; 204:1644-1651.
- Giguère S: *Rhodococcus equi* pneumonia. Proceedings of the 47th Annual Convention of the American Association of Equine Practitioners, pp 456-467, 2001.
- Hillidge CJ: Use of erythromycin-rifampin combination in treatment of *Rhodococcus equi* pneumonia. *Vet Microbiol* 1987; 14:337-342.
- Hoffman AM, Viel L, Juniper E et al: Clinical and endoscopic study to estimate the incidence of distal respiratory tract infection in Thoroughbred foals on Ontario breeding farms. *Am J Vet Res* 1993; 54:1602-1607.
- Hoffman AM, Viel L, Prescott JF et al: Association of microbiologic flora with clinical endoscopic, and pulmonary cytologic findings in foals with distal respiratory tract infection. *Am J Vet Res* 1993; 54:1615-1622.
- Madigan JE, Hietala S, Mueller N: Protection against naturally acquired *Rhodococcus equi* pneumonia in foals by administration of hyperimmune plasma. *J Reprod Fertil* 1991; 44[Suppl]:S71-S78.
- Martens RJ, Ruoff WW, Renshaw HW: Foal pneumonia: a practical approach to diagnosis and therapy. *Comp Cont Educ Pract Vet* 1982; 9:S361-S375.
- Prescott JF, Hoffman AM: *Rhodococcus equi*. *Vet Clin North Am Equine Pract* 1993; 9:375-384.
- Sellon DC: Investigating outbreaks of respiratory disease in older foals. Proceedings of the 47th Annual Convention of the American Association of Equine Practitioners, pp 447-455, 2001.
- Sweeney CR, Sweeney RW, Divers TJ: *Rhodococcus equi* pneumonia in 48 foals: response to antimicrobial therapy. *Vet Microbiol* 1987; 14:329-336.

CHAPTER 12.9

Bronchointerstitial Pneumonia and Acute Respiratory Distress

W. DAVID WILSON

Davis, California

JEFFREY LAKRITZ

Columbia, Missouri

A sporadic, rapidly progressive, high-mortality, acute respiratory distress syndrome (ARDS) has been described in foals aged between 1 week and 8 months. The syndrome appears to be distinct from the acute respiratory distress syndrome seen in neonatal foals and has been encountered in Canada, the northeastern United States, Florida, Kentucky, Oklahoma, Kansas, California, Britain, Denmark, and France. It probably also occurs elsewhere.

ETIOPATHOGENESIS

This syndrome likely does not have a single etiology but rather represents the common reaction of the lung to a number of different insults, the precise nature of which remains to be determined. A viral etiology has been pro-

posed based on the sporadic nature of the disease, the age incidence, and the histologic lesions, which include multinucleate syncytial cells similar to those seen with bovine respiratory syncytial virus (BRSV) infection in cattle. Although viruses such as influenza virus and equine adenovirus are capable of causing diffuse alveolar damage and although certain strains of equine influenza A-equine-2 virus have been reported to induce severe fatal pneumonitis and respiratory distress in foals, viral agents do not appear to be involved in the majority of cases of ARDS.

Pneumocystis carinii has been implicated as a potential cause of ARDS in foals, based on the identification of this organism in the lungs of a number of fatally affected foals in Britain, the northeastern United States, Canada, Florida, and Japan. This parasite, a unicellular

eukaryote classified as a fungus, is generally thought to be an opportunist pathogen of patients with immune deficiency disorders and is well recognized to commonly infect Arabian foals with severe combined immunodeficiency. The identification of *P. carinii* in the lungs of affected foals—many of which are also infected with *Rhodococcus equi*, an organism now recognized to be a common pathogen of human patients with acquired immunodeficiency syndrome (AIDS)—has led to the suggestion that these foals may be suffering from an as yet undefined immune deficiency state that may involve defective production of gamma interferon by CD4+ lymphocytes. Decreased proportion of CD4+ and CD8+ T lymphocytes has been observed in foals infected with *P. carinii*. The finding that gram-negative enteric organisms such as *Escherichia coli* are also commonly isolated from the lungs of foals with ARDS also supports this concept. In addition, many affected foals were being treated with erythromycin, rifampin, or other antibiotics for a preexisting respiratory infection—often *R. equi* pneumonia—before the onset of signs of ARDS. Recent studies have documented that erythromycin administered orally as erythromycin base causes a profound inhibition of neutrophil migration into pulmonary airways in response to an inflammatory stimulus. This effect likely inhibits phagocytic clearance from the lower airways and may allow proliferation of opportunist pathogens such as *P. carinii* or gram-negative enteric bacteria, which may then contribute to the development of the alveolar, bronchiolar, and interstitial lesions typically found in affected foals. *R. equi* alone can cause apparent acute-onset respiratory distress because the clinical signs associated with the insidious development of pulmonary consolidation and multiple pyogranulomas may go unobserved by owners or because of acute fulminant infection from massive airborne challenge.

The similarity of the pulmonary lesions seen in affected foals to those seen in cattle with atypical interstitial pneumonia (fog fever) has prompted the suggestion that this syndrome may be caused by ingestion of pneumotoxins such as *Perilla* mint ketone, pyrrolizidine alkaloid, paraquat, or 3-methyl indole. However, the lesions produced by the administration of these compounds to horses do not duplicate all the lesions seen in naturally affected foals. The majority of affected foals seen in these authors' clinic have presented during hot weather (usually in excess of 90° F) or after transportation on hot days, thus suggesting that heat stress may play a role. A number of foals were being treated with antibiotics before the onset of signs of severe respiratory distress. Bacterial toxins or mediators produced during the pulmonary response to infection may play a role in the pathogenesis of this condition. In some instances, the condition may represent a pulmonary manifestation of systemic inflammatory response syndrome (SIRS) induced by endotoxin. Direct side effects of the antibiotic treatment should also be considered. For example, horses occasionally develop hyperthermia during courses of treatment with erythromycin. The ability of the foal to dissipate heat during periods of high ambient temperature may be further compromised by underlying bacterial or viral lung disease, thus resulting in a progressive cycle of thermal injury to the lung.

PATHOLOGIC FINDINGS

The lungs of affected foals that die are diffusely red, wet, heavy, firm, and fail to collapse when the chest is opened. In many instances the lungs have a mottled lobulated appearance with dark reddened areas interspersed between areas of more normal-appearing lung tissue. Airway lumens usually contain various amounts of pink foamy fluid, and the cut surface exudes fluid and has edematous separation of lobules. A substantial number of foals also have other lung lesions such as *R. equi* pyogranulomas, which represent preexisting pulmonary disease, and many also show hypoxemia-induced lesions in other organs.

Histopathologic pulmonary lesions include severe, diffuse necrotizing bronchiolitis, alveolar septal necrosis, and filling of alveolar spaces with large numbers of neutrophils and lesser numbers of macrophages, lymphocytes, desquamated pneumocytes, and epithelioid-like cells enmeshed in an eosinophilic proteinaceous to fibrinoid material suggestive of hyaline membranes. Other prominent lesions include congestion and edema of the interstitium, hyperplasia of type II pneumocytes, and, in more chronic cases, interstitial fibrosis. Intracellular viral inclusion bodies are not evident. The relative predominance of lesions differs to some extent between foals and probably reflects the severity and chronicity of the condition, preexisting lung disease, and perhaps the initiating etiologic agent. For instance, diffuse alveolar damage is a prominent early lesion that appears to precede development of necrotizing bronchiolitis, proliferation of type II pneumocytes, and interstitial fibrosis. Although multinucleate syncytial cells are a consistent finding in exudate in foals in which *P. carinii* is present, they are not consistently found in all cases of bronchointerstitial pneumonia.

CLINICAL SIGNS AND DIAGNOSIS

The clinical presentation of affected foals includes an acute or peracute onset of respiratory distress manifested by marked tachypnea, nostril flaring, extended head and neck position, increased intercostal and abdominal effort, and, in many instances, a notable double expiratory lift and "heave line." The majority of affected foals are cyanotic at rest (or become so with minimal exertion) and are febrile, depressed, and reluctant to move or eat. Nasal discharge and cough are frequent but inconsistent findings. Although cough is often part of the history because affected foals often have underlying bacterial pneumonia, the onset of respiratory distress may diminish the frequency of efforts to cough. Thoracic auscultation reveals tachycardia, loud bronchial sounds over central airways, and reduced bronchovesicular sounds in peripheral areas of the lung, thus suggesting reduced ventilation of small airways. Crackles and polyphonic wheezes are heard in the caudodorsal lung fields of those foals that retain sufficient air movement in the lung periphery, and the sounds tend to become more prominent as ventilation improves in response to treatment. This change in auscultation findings appears to have prognostic value because lung sounds in those foals that die tend to remain bronchial and do not show the increase in adventitious sounds heard in recovering foals. The clinical course in foals that do not survive ranges from less than 24 hours—in which case the presentation may be one of apparent sudden

death—to several weeks, although the clinical course is generally less than 7 days.

Laboratory findings include neutrophilic leukocytosis, hyperfibrinogenemia, and hypoxemia with a hypercapnic respiratory acidosis. Laboratory abnormalities that reflect dehydration, diffuse intravascular coagulation, and hypoxic injury to other organs are seen in some foals. Thoracic radiographs typically show prominent interstitial patterns of increased density with superimposed mixed bronchial and alveolar patterns of varying severity distributed diffusely throughout the lung fields. Moreover, radiographic findings may include evidence of an underlying disease process such as consolidating anteroventral pneumonia or diffusely distributed pyogranulomas in foals with concomitant *R. equi* infection. Early in the course of the disease, radiographs may show a diffuse alveolar pattern of increased density that reflects alveolar flooding induced by diffuse alveolar damage. In foals that respond well to treatment, this alveolar pattern resolves over a period of days, but resolution of the prominent bronchointerstitial pattern may be incomplete even after many months. A prominent miliary reticulonodular pattern is found in the majority of foals with *P. carinii* infection but has also been identified in foals with respiratory distress in which *P. carinii* was not identified.

If not precluded by the severity of clinical signs, tracheobronchial aspirates should be collected in an attempt to identify the etiologic agent and guide treatment. In selected cases, bronchoalveolar lavage (BAL) may also prove helpful, particularly for the identification of *P. carinii*. In addition to routine cytologic examination and bacterial culture, efforts should be made to isolate or identify viruses and *P. carinii* in tracheobronchial aspirates or BAL samples (and in pulmonary tissues of foals that die). *P. carinii*—in its trophozoite, sporozoite, and cyst forms—can be identified by Wright's-Giemsa, toluidine blue, or Gomori's methenamine silver—or, optimally, by immunofluorescence staining methods, fluorescent *in situ* hybridization, or electron microscopy.

TREATMENT AND PROGNOSIS

This syndrome constitutes a respiratory emergency that necessitates aggressive and intensive therapy. A variety of treatments have been used, including oxygen by nasal insufflation or transtracheal percutaneous oxygenation, nebulization, antihistamines, bronchodilators, antibiotics, corticosteroids, nonsteroidal antiinflammatory drugs, and external thermoregulation. The high mortality rate in the face of multiple treatments most likely indicates that no single treatment is highly effective, although the administration of corticosteroids and oxygen and management of hyperthermia appear to be very important. Therapeutic outcomes at these authors' clinic have improved considerably since high doses of dexamethasone (0.2 to 0.4 mg/kg IV q24h or q12h) were incorporated into the initial treatment protocol. The use of glucocorticoids is further supported by the finding that the risk of respiratory failure and death in human immunodeficiency virus (HIV)-positive human patients with moderate to severe *P. carinii* pneumonia is reduced by early inclusion of these drugs in the therapeutic regimen. Recognition that *P. carinii* may be involved in some foals suggests that specific treatment with

antimicrobials, such as trimethoprim-sulfonamide combinations (24-36 mg of combination/kg of body weight per day), which inhibit folate synthesis, is indicated. The pulmonary interstitial fibrosis seen in chronic cases and radiographic evidence of a persistent increase in pulmonary interstitial density several months after recovery in a limited number of surviving foals suggest that survival may be accompanied by permanent pulmonary pathology that could potentially impair future performance.

PREVENTION

Until the etiology of this syndrome is better understood, definitive therapeutic and prophylactic recommendations cannot be made. However, the apparent association with heat stress in many cases suggests that particular care should be taken to control ambient temperature and to protect foals—especially those being treated for respiratory disease—against direct exposure to the sun on hot days. Transporting foals during hot weather should be avoided. Necessary transportation should be performed early in the morning when it is cool, and appropriate ventilation of the trailer should be provided. The recognition that erythromycin may interfere with thermoregulation suggests that foals requiring treatment with erythromycin during hot weather should be carefully monitored and kept in the shade during the hottest portion of the day, preferably by confining them in a cool, well ventilated area with fans or air conditioning. Foals that develop hyperthermia should be recognized early and managed aggressively to reduce their core body temperature before severe systemic and pulmonary complications develop. The use of large fans, the application of ice water and alcohol baths, and cold-water enemas in a shaded or air-conditioned area can be lifesaving under these circumstances. Administration of corticosteroids, flunixin meglumine, or other nonsteroidal antiinflammatory drugs to hyperthermic foals may help prevent cell death and secondary effects but does not reverse the hyperthermia unless other measures are instituted.

Supplemental Readings

- Ainsworth DM, Weldon AD, Beck KA et al: Recognition of *Pneumocystis carinii* in foals with respiratory distress. *Equine Vet J* 1993; 25:103-108.
- Buergelt CD, Hines SA, Cantor G et al: A retrospective study of proliferative interstitial lung disease of horses in Florida. *Vet Pathol* 1986; 23:750-756.
- Ewing PJ, Cowell RL, Tyler RD et al: *Pneumocystis carinii* pneumonia in foals. *J Am Vet Med Assoc* 1994; 204:929-933.
- Lakritz J, Watson J, Wilson WD et al: Pulmonary lavage cell populations in foals treated with erythromycin. In *Proceedings of the 11th Veterinary Medical Forum of the American College of Veterinary Internal Medicine*, p 958, 1993.
- Lakritz J, Wilson WD, Berry CR et al: Bronchointerstitial pneumonia and respiratory distress in young horses: clinical, clinicopathologic, radiographic, and pathological findings in 23 cases (1984-1989). *J Vet Intern Med* 1993; 7:277-288.
- Lakritz J, Wilson WD: Erythromycin: pharmacokinetics, bioavailability, nonantimicrobial activity, and possible mechanisms associated with adverse reactions. *Proceedings of the 43rd Annual Convention of the American Association of Equine Practitioners*, pp 83-86, 1997.

Prescott JF: Immunodeficiency and serious pneumonia in foals: the plot thickens. *Equine Vet J* 1993; 25:88-89.

Prescott JF, Wilcock BP, Carman PS et al: Sporadic, severe bronchointerstitial pneumonia of foals. *Can Vet J* 1991; 32:421-425.

Stratton-Phelps M, Wilson WD, Gardner IA: Risk of adverse effects in pneumonic foals treated with erythromycin versus other antibiotics: 143 cases (1986-1996). *J Am Vet Med Assoc* 2000; 217:68-73.

Traub-Dargatz J, Wilson WD, Conboy S et al: Hyperthermia in foals treated with erythromycin alone or in combination with rifampin for respiratory disease during hot environmental conditions. *Proceedings of the 42nd Annual Convention of the American Association of Equine Practitioners*, pp 243-247, 1996.

Whitwell K: *Pneumocystis carinii* infection in foals in the UK. *Vet Rec* 1992; 131:19.

CHAPTER 12.10

Foal Diarrhea

GUY D. LESTER

Perth, Western Australia

Diarrhea is one of the most important medical conditions of foals, in terms of morbidity, mortality, and cost to the owner. Numerous infectious and noninfectious causes of diarrhea in newborn and growing foals exist. Unfortunately, determination of a specific etiology in individual cases continues to be difficult because of our incomplete understanding of normal flora and limitations in available diagnostic tests. The isolation of an organism from the feces of foals with diarrhea may not directly indicate that that agent causes the diarrhea. *Clostridium perfringens* biotype A, *Rhodococcus equi*, *Bacteroides fragilis*, and rotavirus are examples of potential enteric pathogens that may be recovered from the feces in the absence of disease.

FOAL HEAT DIARRHEA

Foal heat diarrhea is arguably the most common cause of diarrhea in young foals. Affected foals are typically aged between 6 and 12 days of age and have a nonfetid, low-volume stool that varies in consistency from soft to watery. The pH of the feces is alkaline. The diarrhea is nondebilitating, and foals remain bright and alert with a good appetite. The basis of foal heat diarrhea is not certain, but likely it is a response to developmental changes within the intestinal tract. The temporal association between coprophagy, the appearance of protozoa in the feces, and the onset of diarrhea implies that the syndrome occurs in response to establishment of intestinal flora. The diarrhea does not appear to be associated with alterations in milk composition, maternal estrus, or parasite infection. Anecdotal reports suggest that the feeding of probiotic preparations may reduce the incidence of foal heat diarrhea.

NUTRITIONAL CAUSES OF DIARRHEA

Diarrhea of nutritional etiology is often seen in orphan foals. However, the quality of commercial milk replacement solutions has improved over recent years, such that

diarrhea is uncommon if the milk is prepared and fed as per the manufacturer's instructions. The feeding of overly dilute or concentrated milk will often cause diarrhea. Many of the commercial replacement products have a greater caloric density than mare's milk, thus necessitating feeding at a volume less than 20% to 25% bodyweight daily. The use of bovine milk is problematic in that it often causes diarrhea and ill-thrift, probably because of its relatively greater proportion of fat. Formulations that use lowfat cow's milk with dextrose have been used with some success. The low complication rate associated with the use of goat's milk is paradoxical given that it has a similar total fat content to bovine milk. The exceptions are mild metabolic derangements seen in some foals and occasional constipation. The fat in goat's milk is more highly emulsified and may be more readily digested by foals.

LACTOSE INTOLERANCE

Primary lactose intolerance is caused by a congenital deficiency or absence of beta-galactosidase (lactase) in the brush border of the small intestine. This form occurs rarely in foals. In contrast, secondary intolerance is a contributing factor to the diarrhea associated with many small intestinal infections. Lactose intolerance should be suspected when diarrhea resolves after withdrawal of milk and then returns when milk is reintroduced. Confirmation is by lactose tolerance test. Briefly, lactose is administered at a dose rate of 1 gm/kg (20% w/v solution) after a 2-hour fast. Blood is sampled before lactose administration and then at 15-minute intervals for 60 minutes. In normal foals the blood glucose concentration should increase by a minimum of 25 mg/dl within 30 minutes. In lactase-deficient foals, glucose rarely increases above 30 mg/dl. Supplementation with lactase (Lactaid caplets or drops [McNeil-PPC, Inc., Ft. Washington, Pa.]; 6000-9000 FCC units every 3 to 6 hours) may have benefit in cases of primary lactose intolerance.

Prescott JF: Immunodeficiency and serious pneumonia in foals: the plot thickens. *Equine Vet J* 1993; 25:88-89.

Prescott JF, Wilcock BP, Carman PS et al: Sporadic, severe bronchointerstitial pneumonia of foals. *Can Vet J* 1991; 32:421-425.

Stratton-Phelps M, Wilson WD, Gardner IA: Risk of adverse effects in pneumonic foals treated with erythromycin versus other antibiotics: 143 cases (1986-1996). *J Am Vet Med Assoc* 2000; 217:68-73.

Traub-Dargatz J, Wilson WD, Conboy S et al: Hyperthermia in foals treated with erythromycin alone or in combination with rifampin for respiratory disease during hot environmental conditions. *Proceedings of the 42nd Annual Convention of the American Association of Equine Practitioners*, pp 243-247, 1996.

Whitwell K: *Pneumocystis carinii* infection in foals in the UK. *Vet Rec* 1992; 131:19.

CHAPTER 12.10

Foal Diarrhea

GUY D. LESTER

Perth, Western Australia

Diarrhea is one of the most important medical conditions of foals, in terms of morbidity, mortality, and cost to the owner. Numerous infectious and noninfectious causes of diarrhea in newborn and growing foals exist. Unfortunately, determination of a specific etiology in individual cases continues to be difficult because of our incomplete understanding of normal flora and limitations in available diagnostic tests. The isolation of an organism from the feces of foals with diarrhea may not directly indicate that that agent causes the diarrhea. *Clostridium perfringens* biotype A, *Rhodococcus equi*, *Bacteroides fragilis*, and rotavirus are examples of potential enteric pathogens that may be recovered from the feces in the absence of disease.

FOAL HEAT DIARRHEA

Foal heat diarrhea is arguably the most common cause of diarrhea in young foals. Affected foals are typically aged between 6 and 12 days of age and have a nonfetid, low-volume stool that varies in consistency from soft to watery. The pH of the feces is alkaline. The diarrhea is nondebilitating, and foals remain bright and alert with a good appetite. The basis of foal heat diarrhea is not certain, but likely it is a response to developmental changes within the intestinal tract. The temporal association between coprophagy, the appearance of protozoa in the feces, and the onset of diarrhea implies that the syndrome occurs in response to establishment of intestinal flora. The diarrhea does not appear to be associated with alterations in milk composition, maternal estrus, or parasite infection. Anecdotal reports suggest that the feeding of probiotic preparations may reduce the incidence of foal heat diarrhea.

NUTRITIONAL CAUSES OF DIARRHEA

Diarrhea of nutritional etiology is often seen in orphan foals. However, the quality of commercial milk replacement solutions has improved over recent years, such that

diarrhea is uncommon if the milk is prepared and fed as per the manufacturer's instructions. The feeding of overly dilute or concentrated milk will often cause diarrhea. Many of the commercial replacement products have a greater caloric density than mare's milk, thus necessitating feeding at a volume less than 20% to 25% bodyweight daily. The use of bovine milk is problematic in that it often causes diarrhea and ill-thrift, probably because of its relatively greater proportion of fat. Formulations that use lowfat cow's milk with dextrose have been used with some success. The low complication rate associated with the use of goat's milk is paradoxical given that it has a similar total fat content to bovine milk. The exceptions are mild metabolic derangements seen in some foals and occasional constipation. The fat in goat's milk is more highly emulsified and may be more readily digested by foals.

LACTOSE INTOLERANCE

Primary lactose intolerance is caused by a congenital deficiency or absence of beta-galactosidase (lactase) in the brush border of the small intestine. This form occurs rarely in foals. In contrast, secondary intolerance is a contributing factor to the diarrhea associated with many small intestinal infections. Lactose intolerance should be suspected when diarrhea resolves after withdrawal of milk and then returns when milk is reintroduced. Confirmation is by lactose tolerance test. Briefly, lactose is administered at a dose rate of 1 gm/kg (20% w/v solution) after a 2-hour fast. Blood is sampled before lactose administration and then at 15-minute intervals for 60 minutes. In normal foals the blood glucose concentration should increase by a minimum of 25 mg/dl within 30 minutes. In lactase-deficient foals, glucose rarely increases above 30 mg/dl. Supplementation with lactase (Lactaid caplets or drops [McNeil-PPC, Inc., Ft. Washington, Pa.]; 6000-9000 FCC units every 3 to 6 hours) may have benefit in cases of primary lactose intolerance.

HELMINTH PARASITES

Infections with helminth parasites are rarely associated with diarrhea in foals. *Strongyloides westeri* infection is unlikely to cause any clinical signs except when present in enormous numbers. Weight loss, ill thrift, and hypoproteinemia have been reported in a 6-month-old foal that was heavily burdened with *S. westeri*. The author suggested that because that foal was raised as an orphan, neonatal exposure to the parasite was probably minimal, thus allowing for increased susceptibility when exposed at an older age. If *S. westeri* has any major importance, it may be as a predisposing factor to enteric pathogens. The parasite is effectively controlled by administration of ivermectin to both mares and foals.

Experimental inoculation of foals with *Strongylus vulgaris* larvae can induce an acute syndrome of fever and diarrhea, but this is unlikely to occur under natural conditions. Small strongyles and ascarids are also not important causes of diarrhea in newborn or growing foals.

PROTOZOAN PARASITES

The role of *Cryptosporidium* in foal diarrhea remains controversial. Infection rates have been reported between 15% and 31% in suckling foals, but the vast majority of these are inapparent infections. Most disease is seen within the first month of life and varies considerably in terms of severity of signs. *Cryptosporidium* has been associated with fatal outcomes in foals, but these are rare. Foals at greatest risk are those with primary immunodeficiencies such as severe combined immunodeficiency (SCID). Clinical infection in immunocompetent animals is self-limiting, but chronic diarrhea has been reported in young foals.

Several methods are used to detect oocysts in fecal samples—including acid-fast or Ziehl-Neelsen staining, immunofluorescence assays, electron microscopy, and flow cytometry. Acid fast staining is very sensitive but is less specific than the other techniques. Submission of fecal samples to a laboratory should specifically state that detection of cryptosporidium is required, as expertise is necessary to detect the small oocysts.

Treatment is generally supportive, and centers on fluid and electrolyte replacement. Specific drug therapy—such as azithromycin or the aminoglycoside paromomycin—could be attempted, but efficacy data in foals are lacking. Prevention includes environmental disinfection and isolation of infected foals.

Giardia infection rates in foals have also been reported to be as high as 35%, but data to associate shedding with disease are also lacking. Isolated cases of suckling foals with diarrhea and high *Giardia* counts that have responded to a short course of metronidazole have been reported. Similarly, *Eimeria leukarti* oocysts are commonly isolated from healthy foals and are not known to cause diarrhea under experimental or natural conditions.

ANAEROBIC BACTERIAL PATHOGENS

Clostridium perfringens biotypes types A and C and *Clostridium difficile* are important causes of enteric disease in young foals. These Gram-positive organisms can be found

in the intestinal tracts of domestic animals and are widely distributed throughout the environment, including the soil. They produce potent exotoxins responsible for a variety of intestinal diseases in domestic animals. Enteric disease induced by *Clostridium* species are recognized more commonly during the early neonatal period, and reports of disease associated with biotypes A, B, C, D, and E exist; however, biotypes A and C are the most important.

Disease induced by *C. perfringens* biotype C is associated with hemorrhagic diarrhea, abdominal distention, colic, circulatory shock, and a high mortality. Death may occur before diarrhea is passed. Disease often occurs within the first 48 hours of life and is most commonly seen in vigorous foals with a high milk intake. The diagnosis is confirmed by mouse inoculation to identify toxin within the feces or intestinal lumen. Recovery of the organism and biotyping through toxin gene identification (PCR) may increase the accuracy of diagnosis short of toxin identification.

Treatment is often unrewarding but should consist of antimicrobial agents including potassium or sodium penicillin and metronidazole, nonsteroidal antiinflammatory agents, plasma or hydroxyethyl starch (10 ml/kg), and *C. perfringens* biotype C antitoxin. Parenteral nutrition should be considered in any aggressive treatment plan (see Chapter 12.6: "Neonatal Septicemia"). Probiotics may be beneficial as part of a treatment protocol or, more importantly, as a preventative strategy in other newborn foals on the property. Anecdotal success has been reported with the use of commercial types C and D toxoid in pregnant mares.

In recent years, enteric disease has emerged in newborn foals and has been attributed to *C. perfringens* biotype A. Clinical signs are more variable but may include transient bloody stool, colic, and fever. Mortality is less than with disease induced by biotype C. The role of biotype A is often confounded because it appears to be commonly present in the feces of healthy young foals as early as 24 hours of age. It is not uncommon for this biotype to produce an enterotoxin (CPE) that can be identified with a commercial fecal assay. Several factors confound the interpretation of this test. Firstly, the toxin is rapidly degraded in fecal samples, and delays in processing will frequently yield a negative result. Secondly, *C. perfringens* species other than biotype A can produce enterotoxin. Lastly, recent information indicates that many biotype A isolates from foals lack the gene to produce enterotoxin. Currently, the most appropriate method of diagnosis involves signalment and clinical signs. Large numbers of Gram-positive rod-shaped bacteria are seen on fecal Gram stain. Spore stains can be requested but rarely provide useful additional data. The isolation of *C. perfringens* biotype A from feces or blood culture increases the accuracy of diagnosis. All *C. perfringens* isolates contain an alpha toxin. Further separation into biotypes A through E is based on identification of additional toxins produced by the bacteria. The exception is a *C. perfringens* isolate that contains the alpha toxin and a β 2 toxin. This organism has been isolated from both adult horses and foals with diarrhea. The future development of commercial fecal toxin tests for α , β 1, and β 2 toxins would provide a clearer insight into the role of *C. perfringens* biotypes in neonatal diarrhea.

The role of *C. difficile* in juvenile diarrhea is also unclear. A well defined cause of neonatal enterocolitis in foals less than 4 days of age, this organism has received a lot of attention in recent years as an enteric pathogen of adult horses. Prevalence varies with geographic location, but *C. difficile* appears to be a rare isolate in older suckling foals. The isolation of *C. difficile* is usually considered significant in foals of all ages, but it is not uncommon to identify foals that are culture positive but toxin negative by ELISA. Fecal samples for culture should be collected and shipped in an appropriate container (Port-a-Cul anaerobic tubes, Becton, Dickinson and Co., Franklin Lakes, N.J.). Commercial assays for toxins A or B of *C. difficile* are reliable if the samples are shipped directly to a diagnostic laboratory or transported on ice and shipped overnight. Treatment is as for *C. perfringens* biotype C with the exception of commercial Type C and D antitoxin.

It is probable that *Bacteroides fragilis*, a gram-negative anaerobic rod, is an intestinal pathogen of foals. Unfortunately isolation of the organism from feces does not confirm diagnosis because the bacterium occurs in both enterotoxigenic and nontoxigenic forms. Pathogenic strains are noninvasive, but produce a ~20 kD heat-labile toxin that induces mucosal inflammation. Limited data from foals suggest that *B. fragilis* is often isolated with other potential enteric pathogens. The diagnosis is made by culture of the organism and then verification of toxin-producing strains by arbitrarily primed PCR or more traditionally through isolated intestinal loop inoculation. Treatment involves administration of metronidazole and supportive therapy.

AEROBIC OR FACULTATIVE ANAEROBIC BACTERIAL PATHOGENS

Escherichia coli is the most common cause of systemic sepsis in newborn foals but is an uncommon primary enteric pathogen. Reports suggest that *E. coli* can mediate a profuse but nonfetid diarrhea in foals less than one month of age. The recovery of *E. coli* from feces is very common, but these isolates typically lack the appropriate virulence factors required to create intestinal disease. The diagnosis is achieved by culture from feces and detection of virulence factors by PCR. A heavy growth of a mucoid *E. coli* on agar plates would increase the level of suspicion.

Outbreaks of salmonellosis can occur in horses of any age, including newborns, but most foal infections occur as isolated cases. The mare appears to be the primary source of infection, and both dam and foal are usually fecal-positive. Rarely do both demonstrate signs of disease. Affected foals usually have moderate to severe clinical signs that include fever, diarrhea, dehydration, profound depression, and reduced appetite. Diarrhea can vary in both consistency and volume and rarely may contain blood. Colic is common in the early stages of the disease. As consequence to bacteremia, *Salmonella* infection in foals less than 2 months of age commonly causes problems such as bacterial uveitis, infectious synovitis, osteomyelitis, pneumonia, and meningitis. A complete blood count usually reveals neutropenia, with a left shift and toxicity, but it is replaced by a neutrophilia as the disease becomes chronic. The fibrinogen concentration is usually elevated.

The diagnosis of *Salmonella* infection is traditionally made by fecal culture. Samples should be transported using suitable transport media (e.g., Ames aerobic culture media). Samples can be transported in selenite broth if processed within 24 hours of collection. Blood culture is worthwhile in foals less than 2 months of age. Fecal PCR appears to be highly sensitive, and a positive result may carry greater importance in a foal than adult horse with diarrhea.

In contrast to adults, most foals with salmonellosis require aggressive and early antibiotic treatment. Commonly used antibiotics include third-generation cephalosporins and aminoglycosides, but selection should be guided by multiple factors—including antimicrobial sensitivity, drug cost, toxicity, and intracellular activity. Unfortunately, secondary sites of infection, particularly osteomyelitis, may develop and persist in the presence of antibiotic therapy, particularly aminoglycosides. These complications may not be detected until weeks after the onset of enteric disease. Fluoroquinolone antibiotics have very good efficacy but should be used with caution given their apparent damaging effects on cartilage.

Enterococcus durans is commonly isolated from the feces of young foals with diarrhea, although often with other potential pathogens. The organism can colonize small intestinal mucosa and induce mild-to-moderate pathology. The severity of diarrhea is inversely related to age. *Rhodococcus equi* infection of the respiratory tract is often associated with changes within the Peyer's patches and mesenteric lymph nodes, but diarrhea is rare. A well defined syndrome of ulcerative enterocolitis attributed to *R. equi* exists, but establishing an *ante mortem* diagnosis is difficult because fecal culture of the organism is common even in normal foals. Other aerobic bacteria implicated in infectious diarrheas include *Aeromonas hydrophila*, *Yersinia enterocolitica*, and *Campylobacter* species.

An emerging intestinal disease of late suckling foals is caused by *Lawsonia intracellularis*. The organism induces proliferation of small intestinal crypt epithelial cells, leading to epithelial hyperplasia, with elongation and branching of crypts of blunting of the villi. Clinical signs include diarrhea, dependent edema, colic, and failure to thrive. Most cases follow a stressful event, such as deworming or vaccination 1 to 3 weeks before presentation. Laboratory data support a protein-losing enteropathy. Thickening of the small intestine is seen on abdominal ultrasound. The definitive diagnosis of *Lawsonia* infection is difficult in the live animal. Detection of bacteria by PCR in the feces or by indirect fluorescent antibody testing on serum is used, but sensitivity and specificity data are lacking. Foals may spontaneously recover, but most require therapy that includes plasma and antibiotics—including metronidazole, chloramphenicol, erythromycin, or azithromycin.

VIRAL INTESTINAL DISEASE

Group A rotavirus is the most common cause of infectious diarrhea in foals. Several foals are typically affected over a short period of time. The disease is highly contagious and has a very short incubation period. The severity of disease is determined by immune status, inoculation dose, and age. The basis of the diarrhea is not fully known but likely

involves brush border enzyme deficiency, thus leading to inadequate digestion of substrate and osmotic diarrhea in the colon. Recent attention has been given to the membrane-spanning nonstructural glycoprotein, NSP4, as a potential viral cytotoxin and enterotoxin. The enterotoxin is released from rotavirus-infected enterocytes and is a specific noncompetitive inhibitor of the Na-glucose symporter. The protein also enhances chloride secretion.

The diagnosis of rotavirus is based on epidemiologic findings of a large number of cases, physical examination findings—including diarrhea, depression, reduced appetite, and low-grade fever—and submission of samples from representative animals. Fecal antigen tests (e.g., Virogen Rotatest or Rotazyme; Abbott Diagnostics, Abbott Park, Ill.) are sensitive and provide rapid confirmation. Electron microscopy is also an effective means of establishing a diagnosis.

The treatment of rotaviral diarrhea supports using a combination of intravenous and oral replacement fluids. Bismuth subsalicylate is commonly used in foals with rotaviral diarrhea. Its antidiarrheal action is through stimulation of fluid and electrolyte absorption and by inhibiting the synthesis of prostaglandins. Bismuth subsalicylate also binds bacterial toxins and is thought to have a bactericidal action. Antibiotics are not indicated unless the foal is less than 2 weeks of age. Affected foals should be isolated if possible because the disease is highly contagious among young foals. Phenol-based disinfectants should be used as footbaths and for environmental decontamination. A maternal vaccine is available and may confer modest protection.

An association between viral enteritis and gastroduodenal ulcer syndrome (GDUD) continues to be suggested. Many foals with GDUD have a history of diarrhea before the onset of more classic signs of ulcers—including bruxism, ptyalism, and colic. It is not uncommon for foals to develop duodenitis, again suggesting an infectious etiology.

Recent reports of coronavirus acting as a primary pathogen in young immunocompetent foals have been published. Previously, foals with immune dysfunction, such as SCID Arabian foals, were considered to be at greatest risk. It is unlikely that coronavirus infection is responsible for outbreaks of diarrhea. Both published and nonpublished reports of parvovirus and Breda virus causing diarrhea in foals exist.

Supplemental Readings

- Lewis LD: Growing horse feeding and care. In Lewis LD (ed): *Equine Clinical Nutrition*, Media, Pa, Williams & Wilkins, 1995.
- Sarma PN, Tang YJ, Prindiville TP et al: Genotyping of *Bacteroides fragilis* isolates from stool specimens by arbitrarily-primed-PCR. *Diagn Microbiol Infect Dis* 2000; 37:225-229.
- Tzipori S, Hayes J, Sims L et al: *Streptococcus durans*: an unexpected enteropathogen of foals. *J Infect Dis* 1984; 150:589-593.
- Walker RL, Madigan JE, Hird DW et al: An outbreak of equine neonatal salmonellosis. *J Vet Diagn Invest* 1991; 3:223-227.
- Weese JS, Staempfli HR, Prescott JF: A prospective study of the roles of *Clostridium difficile* and enterotoxigenic *Clostridium perfringens* in equine diarrhoea. *Equine Vet J* 2001; 33:403-409.

CHAPTER 12.11

Colic in Foals

SUSAN J. HOLCOMBE
East Lansing, Michigan

Acute abdominal disease in the foal is a common problem with a myriad of potential causes and presentations. The foal may appear healthy and show signs of mild abdominal discomfort, or it may experience extreme pain and exhibit signs of endotoxic and hypovolemic shock. Resuscitation should be started immediately for the critical foal before or concurrently with diagnostic testing. A colicky foal is more difficult to evaluate than an adult horse; foals are less tolerant of abdominal pain, and the degree of pain exhibited does not necessarily correlate with the severity of the abdominal lesion. Although rectal palpation cannot be used, abdominal radiography and ultrasonography are very useful tools for evaluating foals with colic. A tentative diagnosis often can be obtained from a thorough history and physical examination. Diagnostic tests—such as venous blood gases, complete blood count (CBC), serum chemistry pro-

file, serum IgG, nasogastric intubation, peritoneal paracentesis, abdominal radiography and ultrasonography, and gastroscopy and duodenoscopy—can provide additional information. Treatment ranges from careful monitoring and medical therapy to surgical intervention.

SIGNALMENT

The signalment of the foal (age, breed, and gender) may provide information important in diagnosing the cause of a colic episode. Meconium impaction, congenital abnormalities, and uroperitoneum are the most frequent causes of colic in neonatal foals. The most common of these is meconium impaction. Meconium is composed of glandular secretions from the gastrointestinal tract, amniotic fluid, and cellular debris and should be passed by 48 hours of age. Foals with meconium impactions show signs of ab-

involves brush border enzyme deficiency, thus leading to inadequate digestion of substrate and osmotic diarrhea in the colon. Recent attention has been given to the membrane-spanning nonstructural glycoprotein, NSP4, as a potential viral cytotoxin and enterotoxin. The enterotoxin is released from rotavirus-infected enterocytes and is a specific noncompetitive inhibitor of the Na-glucose symporter. The protein also enhances chloride secretion.

The diagnosis of rotavirus is based on epidemiologic findings of a large number of cases, physical examination findings—including diarrhea, depression, reduced appetite, and low-grade fever—and submission of samples from representative animals. Fecal antigen tests (e.g., Virogen Rotatest or Rotazyme; Abbott Diagnostics, Abbott Park, Ill.) are sensitive and provide rapid confirmation. Electron microscopy is also an effective means of establishing a diagnosis.

The treatment of rotaviral diarrhea supports using a combination of intravenous and oral replacement fluids. Bismuth subsalicylate is commonly used in foals with rotaviral diarrhea. Its antidiarrheal action is through stimulation of fluid and electrolyte absorption and by inhibiting the synthesis of prostaglandins. Bismuth subsalicylate also binds bacterial toxins and is thought to have a bactericidal action. Antibiotics are not indicated unless the foal is less than 2 weeks of age. Affected foals should be isolated if possible because the disease is highly contagious among young foals. Phenol-based disinfectants should be used as footbaths and for environmental decontamination. A maternal vaccine is available and may confer modest protection.

An association between viral enteritis and gastroduodenal ulcer syndrome (GDUD) continues to be suggested. Many foals with GDUD have a history of diarrhea before the onset of more classic signs of ulcers—including bruxism, ptyalism, and colic. It is not uncommon for foals to develop duodenitis, again suggesting an infectious etiology.

Recent reports of coronavirus acting as a primary pathogen in young immunocompetent foals have been published. Previously, foals with immune dysfunction, such as SCID Arabian foals, were considered to be at greatest risk. It is unlikely that coronavirus infection is responsible for outbreaks of diarrhea. Both published and nonpublished reports of parvovirus and Breda virus causing diarrhea in foals exist.

Supplemental Readings

- Lewis LD: Growing horse feeding and care. In Lewis LD (ed): *Equine Clinical Nutrition*, Media, Pa, Williams & Wilkins, 1995.
- Sarma PN, Tang YJ, Prindiville TP et al: Genotyping of *Bacteroides fragilis* isolates from stool specimens by arbitrarily-primed-PCR. *Diagn Microbiol Infect Dis* 2000; 37:225-229.
- Tzipori S, Hayes J, Sims L et al: *Streptococcus durans*: an unexpected enteropathogen of foals. *J Infect Dis* 1984; 150:589-593.
- Walker RL, Madigan JE, Hird DW et al: An outbreak of equine neonatal salmonellosis. *J Vet Diagn Invest* 1991; 3:223-227.
- Weese JS, Staempfli HR, Prescott JF: A prospective study of the roles of *Clostridium difficile* and enterotoxigenic *Clostridium perfringens* in equine diarrhoea. *Equine Vet J* 2001; 33:403-409.

CHAPTER 12.11

Colic in Foals

SUSAN J. HOLCOMBE
East Lansing, Michigan

Acute abdominal disease in the foal is a common problem with a myriad of potential causes and presentations. The foal may appear healthy and show signs of mild abdominal discomfort, or it may experience extreme pain and exhibit signs of endotoxic and hypovolemic shock. Resuscitation should be started immediately for the critical foal before or concurrently with diagnostic testing. A colicky foal is more difficult to evaluate than an adult horse; foals are less tolerant of abdominal pain, and the degree of pain exhibited does not necessarily correlate with the severity of the abdominal lesion. Although rectal palpation cannot be used, abdominal radiography and ultrasonography are very useful tools for evaluating foals with colic. A tentative diagnosis often can be obtained from a thorough history and physical examination. Diagnostic tests—such as venous blood gases, complete blood count (CBC), serum chemistry pro-

file, serum IgG, nasogastric intubation, peritoneal paracentesis, abdominal radiography and ultrasonography, and gastroscopy and duodenoscopy—can provide additional information. Treatment ranges from careful monitoring and medical therapy to surgical intervention.

SIGNALMENT

The signalment of the foal (age, breed, and gender) may provide information important in diagnosing the cause of a colic episode. Meconium impaction, congenital abnormalities, and uroperitoneum are the most frequent causes of colic in neonatal foals. The most common of these is meconium impaction. Meconium is composed of glandular secretions from the gastrointestinal tract, amniotic fluid, and cellular debris and should be passed by 48 hours of age. Foals with meconium impactions show signs of ab-

dominal pain within 6 to 24 hours of birth. Colts are somewhat more predisposed than fillies because the pelvis is narrower in colts.

Congenital atresia of the colon, rectum, or anus is rare. Colonic atresia occurs twice as often as rectal or anal atresia in horses. Foals with colonic atresia pass no meconium, develop abdominal distention, and show signs of abdominal pain between 12 and 24 hours of age. Surgical intervention can be successful in some cases of gastrointestinal atresia, but these foals should be evaluated for other congenital abnormalities, including rectovaginal fistulas in fillies, rectourethral fistulas in colts, anomalies of the sacral and coccygeal vertebrae, and renal hypoplasia. Paint foals that are primarily white and whose dam and sire are overo are at risk for ileocolonic aganglionosis or lethal white syndrome. These foals appear normal at birth but begin to show signs of abdominal pain and distention by 24 hours of age. They pass no meconium, and no fecal staining appears on thermometers or enema tubes. No treatment for lethal white syndrome exists because the myenteric ganglia are absent from the ileum, cecum, and/or colon.

Foals with ruptured bladders usually begin to show clinical signs of uroabdomen by 24 to 72 hours of age. Ruptured bladder is the most common cause of uroabdomen in foals and is more common in colts because the urethra is narrower. These foals "flag" their tails, are restless, and strain to urinate. Clinical signs will develop more slowly (4-7 days) in foals with ruptured or torn ureters. No sex predilection exists, but these foals may have some history of trauma at birth.

Intussusceptions are most common in 3- to 5-week-old foals. Small intestinal volvulus, ascarid impaction, and some colonic abnormalities typically occur in foals 2 to 5 months of age. Fecaliths of the large and small colon are more common in miniature horse and pony foals, but they can occur in any breed.

HISTORY

Information regarding the duration of colic, the degree and progression of pain, passage of feces and urine, consistency of feces, appetite, and medication given is critical in determining the likely cause and any potential secondary problems. Gastric and/or duodenal ulcers are a common complication if a foal has had previous health problems, or has received nonsteroidal antiinflammatory drugs. Previous illness on the farm may increase the suspicion of an infectious etiology such as *Salmonella* sp., *Clostridia* sp., rotavirus, enteritis, or enterocolitis. Abdominal abscesses can occur in older foals with a history of *Streptococcus* sp. or *Rhodococcus equi* pneumonia. A history of recent (7-10 days) anthelmintic treatment is seen in cases of ascarid impaction of the small intestine. Information about the periparturient events may be important when evaluating neonatal foals with colic. Abdominal adhesions may be the cause of colic in foals with a history of previous abdominal surgery.

PHYSICAL EXAMINATION

Subjective evaluation of the foal is important. Assessing the degree and progression of pain and the response to analgesic medication will help determine therapeutic plans and with surgical decision making. Signs of severe

pain include rolling and thrashing. More moderate signs of pain include pawing, restlessness, lying down, and abnormal postures. Foals with meconium impactions strain to defecate by posturing with the hind limbs placed beneath them and tail flagging with the back dorsiflexed. When foals are straining to urinate, their postures are more ventroflexed with the hind limbs stretched out behind them. If the foal is still with the mare, the examiner should note the frequency and intensity of nursing. Foals with gastric ulceration may roll up onto their backs or exhibit bruxism and sialorrhea, especially after nursing.

The foal's abdominal contour may help determine the cause of the colic episode. Foals will appear bloated if they have colonic gas accumulation caused by meconium impaction, peritoneal fluid accumulation from ascites or urine, or small or large intestinal fluid accumulation caused by enteritis. Measuring with a tape or rope the abdominal circumference can monitor progression or regression of abdominal distention. Marking the dorsum and ventrum of the foal—where the tape is placed—with an indelible marker or clipping some hair helps to ensure consistent measurement.

After observing the foal's behavior, the foal should be lightly restrained for the physical examination. Hydration and perfusion should be assessed. Signs of poor perfusion include increased capillary refill time (>2 seconds); cold ears, muzzle, and extremities; and elevated heart rate. The presence of sunken eyes and dry, sticky mucus membranes is evidence of moderate to severe dehydration. An elevated temperature (>102° F) may indicate an infectious cause of the colic episode, such as bacterial or viral enteritis. Hypothermia is rare but often indicates poor perfusion, hypoglycemia, or hypodynamic shock. Thoracic auscultation should be performed on the right and left sides of the thorax to evaluate the heart and lungs. Mean heart rate is 100 beats per minute during the first 30 days of life and decreases to 60 to 70 beats per minute by 2 to 3 months. Elevated heart rate may occur in response to pain, excitement, hypovolemia, or endotoxemia. Bradycardia is rare but may occur in foals with uroabdomen, if they are hyperkalemic (serum $[K^+]$ >5.5 mEq/dl). These foals are also prone to cardiac arrhythmias. Cardiac murmurs may be normal in foals up to 3 to 5 days of age and are usually caused by blood flow through a patent ductus arteriosus. Fever and anemia can also produce cardiac murmurs. The lungs should be auscultated on the right and left sides and over the trachea. Borborygmi audible within the thorax are normal because of the shape of the diaphragm and do not indicate diaphragmatic hernia.

The abdomen can be auscultated, balloted, palpated, and percussed. Progressive borborygmi are produced by gas and fluid interfaces within the gastrointestinal tract. The presence of borborygmi is usually considered normal. However, foals with gastrointestinal obstruction initially will have borborygmi of increased intensity that is followed by a period of decreased to absent intestinal sounds, thus indicating decreased gastrointestinal motility or ileus. Increased intensity of borborygmi may indicate enteritis. Percussing the abdomen and listening for a ping sound can detect gas distention of the cecum and large colon. Palpation of the umbilicus and inguinal area is performed to identify hernias. Many reducible umbilical and inguinal hernias are found incidentally during the physical examination, but if

pain is elicited during palpation or if the hernia is not reducible, surgery is usually indicated.

NASOGASTRIC INTUBATION

A nasogastric tube is passed into the stomach to facilitate decompression of gas and/or fluid. Siphoning with small amounts of water (60 ml) can be used to collect gastric fluid. Net gastric reflux indicates some impediment to gastric emptying. This may be a functional (e.g., ileus or enteritis) or mechanical obstruction (e.g., small intestinal volvulus). Ileus can result from overfeeding in neonatal foals—especially premature or dysmature foals.

ABDOMINAL ULTRASONOGRAPHY

Ultrasonography is an extremely useful tool for evaluating abdominal contents and intestinal motility in foals. The examination can be performed with the foal standing or in lateral recumbency. If the hair coat is thick, the hair

on the abdomen should be clipped to obtain diagnostic images. If the hair coat is thin, liberal application of alcohol often suffices. In most foals, a 5.0- to 7.5-MHz transducer will provide sufficient depth to image the abdomen. Large volumes of anechoic free fluid within the abdomen may indicate uroabdomen or ascites. If the fluid is more hyperechoic with debris, septic peritoneal fluid may be suspected. The motility and contents of the small and large intestine can be assessed. Normal small intestine should be motile with very little content. Large, taut, circular loops may indicate small intestinal physical obstruction (Figure 12.11-1).

However, foals with enteritis commonly also have distended small intestinal loops. Small intestinal intussusceptions have a bull's-eye or target appearance in cross section (Figure 12.11-2). Masses such as ascarid impaction or foreign body can sometimes be imaged. Both the large colon and small intestine may be fluid-filled—with hypermotility or hypomotility—in foals with enteritis. Meconium impactions can sometimes be seen as echogenic masses

Figure 12.11-1 Ultrasonographic image of the abdomen of a foal with a small intestinal volvulus. Notice the taut, round, small intestinal loops.

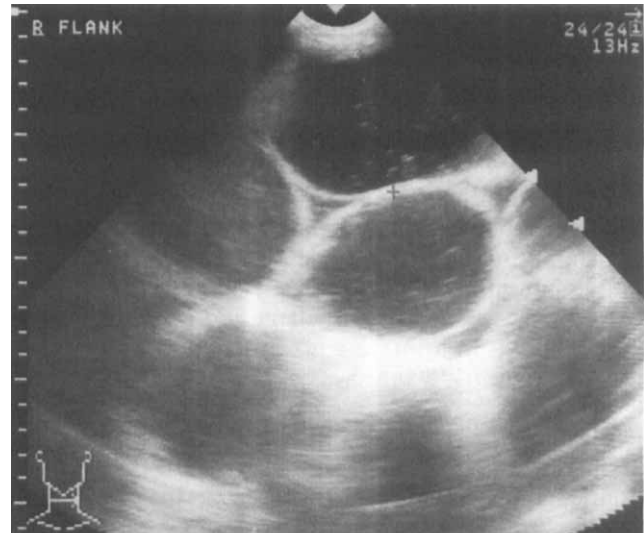


Figure 12.11-2 Ultrasonographic image of the abdomen of a foal with an ileocecal intussusception. Notice the bull's-eye formed by the intussusceptum and intussusciens within the cecum.



within the small colon (Figure 12.11-3). Inguinal hernias can be confirmed by intestinal loops within the scrotum.

ABDOMINAL RADIOGRAPHY

Radiographs can provide valuable information about abdominal lesions in foals. In general, large colon and small intestinal gas distention (Figure 12.11-4), meconium impactions (see Figure 12.11-3), fecaliths, foreign bodies (Figure 12.11-5), and abdominal fluid can be seen.

Portable radiographic equipment can be used to take abdominal radiographs of foals. Technique depends on

the machine. Lateral views can be taken using 14- × 17-inch cassettes in recumbent or standing foals. Dorsoventral views can be helpful, especially to image the transverse colon during a contrast study. However, dorsoventral views can be difficult and sometimes dangerous to obtain if the foal has abdominal distention.

Contrast studies—including barium enemas and upper gastrointestinal series—can be performed to help diagnose meconium impactions, gastrointestinal atresia, and gastric emptying defects caused by pyloric stenosis and duodenal ulceration, respectively. A barium enema can be performed in a standing or recumbent foal. Mild sedation is

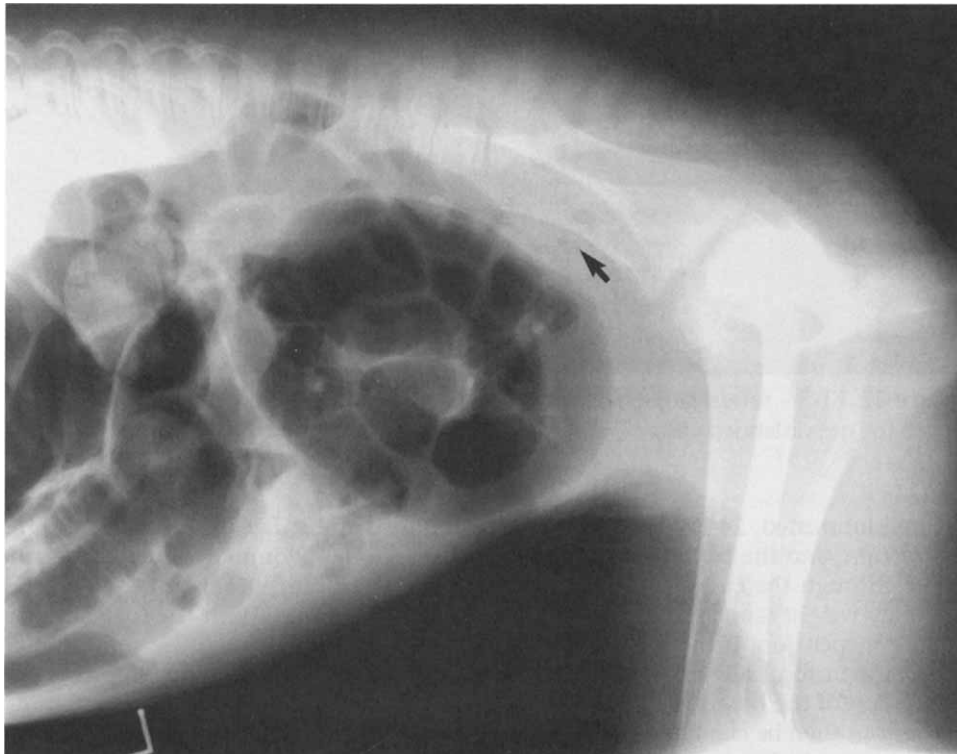


Figure 12.11-3 Lateral radiograph of the abdomen of a foal with meconium impacted in the small colon and rectum (*arrow*). Notice the generally gas-distended small intestine and large colon.

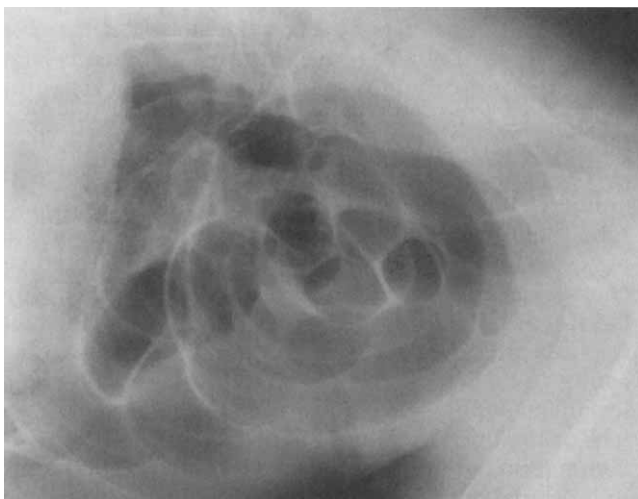


Figure 12.11-4 Lateral radiograph of the abdomen of a foal with a small intestinal volvulus. Notice the taut, erectile intestinal loops.

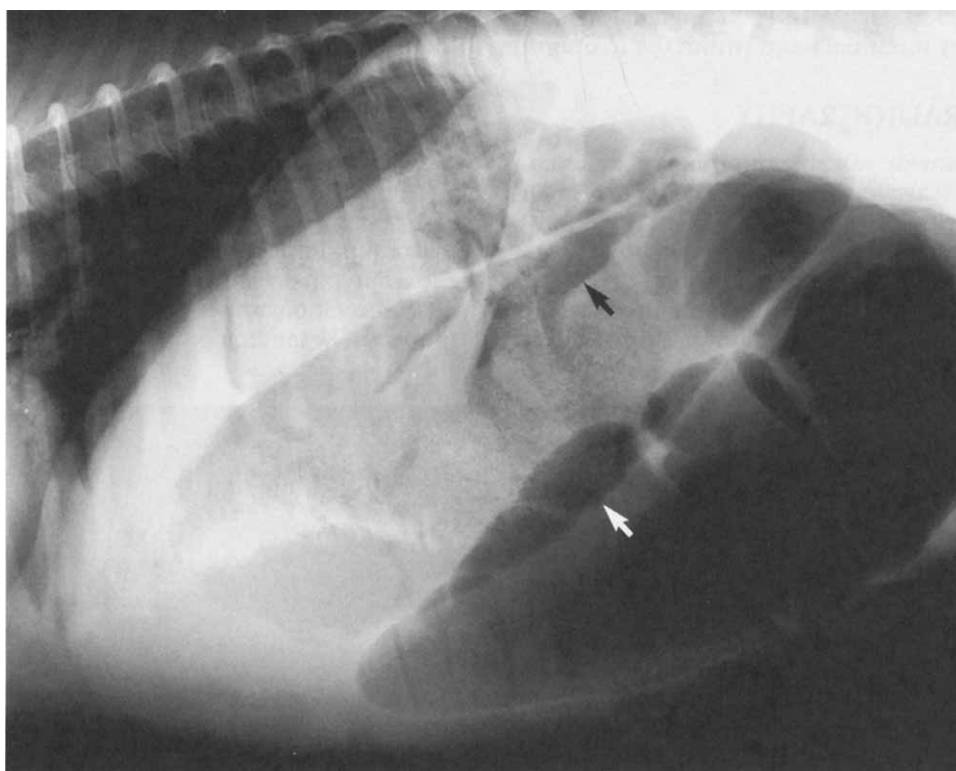


Figure 12.11-5 Lateral radiograph of the abdomen of a foal with a colonic sand impaction. Notice the gas-distended cecum (*white arrow*) and impacted large colon (*black arrow*).

usually indicated. A well lubricated, 24-Fr Foley catheter is advanced into the rectum, and the balloon is inflated. Barium can be infused through the catheter, by gravity flow, up to 20-ml/kg-body weight (approximately 1 L) of 30% w/v barium sulfate suspension. If the foal struggles or if the barium sulfate suspension leaks around the Foley catheter, the administration of the barium should be discontinued. The catheter can then be clamped, and lateral and dorsoventral radiographs can be obtained. In a study of 25 foals with colic in which barium enemas were given, the technique was 100% sensitive and 100% specific for identifying small colon and transverse colon obstructions. The technique had slightly less sensitivity and specificity for identifying large colon lesions but was very helpful for ruling in or out colonic atresia.

Upper gastrointestinal contrast studies can be performed in foals where a gastric emptying defect is suspected. Following nasogastric intubation, 5 ml/kg of 30% w/v barium sulfate can be administered by gravity flow. Radiographs should be taken at time 0, 15, and 30 minutes and then every hour until the barium has reached the small colon. The stomach should be empty within 2 hours of barium administration in normal foals. Upper gastrointestinal contrast studies should not be performed on foals with small intestinal distention.

PERITONEAL FLUID ANALYSIS

Analysis of peritoneal fluid for color, clarity, total protein, cellularity, and cytology can aid in assessment of the viability of the gastrointestinal tract. Foals should be re-

strained and sedated lightly for this procedure to prevent damage to abdominal viscera. Ultrasonography is useful to find a fluid pocket or can be used to guide the abdominocentesis. With the foal standing or in lateral recumbency, an area on the ventral abdomen—caudal to the xyphoid, on midline or slightly to the right—is clipped and prepared in a sterile manner. A subcutaneous bleb of lidocaine or mepivacaine hydrochloride should be used to anesthetize the skin. A 20-g needle or teat canula can be used. If a teat canula is used, a stab incision is made through the skin with a number 15 scalpel blade, and the teat canula is advanced through the body wall. One study showed no statistical difference in the likelihood of enterocentesis between a needle and a teat canula, but some clinicians feel that use of the teat canula is safer. However, because the penetrating hole into the abdomen is larger when the teat canula is used, evisceration of omentum may occur. If enterocentesis occurs, the foal should be placed on broad-spectrum antibiotics for 7 to 10 days.

The peritoneal fluid can be collected in an ethylenediaminetetraacetic acid (EDTA) tube and a clot or red top tube if fluid culture is indicated and should be analyzed for color and clarity, total protein, total nucleated cell count, γ -glutamyl transferase (GGT), creatinine, glucose, lactate, phosphate, and pH. Normal total protein values for foals are 0.7 to 2.3 g/dl. Normal total nucleated cell counts in foals are lower than adult horses and should be less than 1,800/ μ l. Elevations in peritoneal fluid total protein or total nucleated cell count indicate abdominal inflammation, which can be caused by enteritis, peritonitis, or intestinal incarceration. Serosanguineous fluid with el-

evated total protein or total nucleated cell count may indicate intestinal incarceration or enteritis. Elevated total nucleated cell count with degenerative neutrophils—with or without visible bacteria—may occur with septic peritonitis. Low pH (<7.2) and elevations in lactate and large dispersions in systemic serum glucose; peritoneal fluid glucose (>50 mg/dl) may indicate septic peritonitis. Blood contamination does not affect total nucleated cell count or protein concentration but will increase the total RBC. Phosphate greater than 3.6 mg/dl predicts major intestinal injury 77% of the time. A ratio of 2:1—peritoneal fluid creatinine:serum creatinine—diagnoses uroabdomen. The peritoneal fluid GGT will be elevated in foals with liver lobe torsion, which is extremely rare. False positive results are uncommon with peritoneal fluid analysis. However, false negative results are more common, thus suggesting that normal peritoneal fluid analysis does not rule out the presence of compromised intestine.

GASTROSCOPY AND DUODENOSCOPY

Gastric and duodenal ulcers can be diagnosed by gastroscopy and duodenoscopy. The stomach and duodenum can be accessed in most foals up to 1 month old with a 1-m endoscope. For foals 1 to 5 months old, a 2-meter endoscope is needed; for foals over 6 months of age, a 3-m endoscope must be used to evaluate the stomach and duodenum. Solid food should be withheld for 12 to 24 hours before the procedure; if possible, liquids should be restricted for 2 to 4 hours. Young foals should be sedated with a combination of diazepam and butorphanol, and older foals can be sedated with xylazine. With the foal appropriately restrained, the endoscope is passed into the esophagus. The margo plicatus can be seen dividing the squamous and glandular portions of the stomach.

The squamous portion is light pink to white, and the glandular portion appears red. The cardia, lesser curvature of the stomach, and margo plicatus should be examined for ulcers (Figure 12.11-6). The pylorus is ventral to the cardia. If the stomach is empty, some of the air should be deflated from the stomach, and the endoscope should be advanced through the pylorus into the duodenum. Pyloric ulceration and stenosis can be diagnosed by examining this area. Care should be taken not to overinflate the stomach, especially in neonatal foals. If the foal shows signs of discomfort, allowing some air to escape should deflate the stomach.

TREATMENT

Fluid Therapy

Foals with acute abdominal disease may be dehydrated or septic or may be in hypovolemic or endotoxic shock. Major fluid shifts can occur as a result of hypersecretion or the systemic effects of endotoxemia. These fluid shifts occur at the expense of the plasma volume—thus resulting in hemoconcentration, decreased circulating volume, and hypovolemia. Appropriate supportive therapy needs to be instituted as soon as possible—at times, before completion of the examination and diagnostic testing. Endotoxin can cause redistribution of up to 20% of the plasma volume

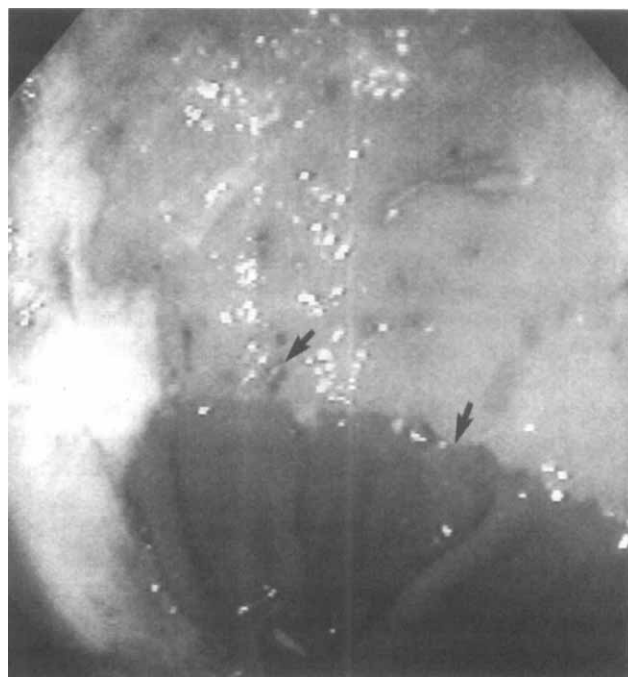


Figure 12.11-6 Gastroscopic image of a foal's stomach. Notice the light-pink squamous portion of the stomach (*top*) and the red glandular portion (*bottom*) divided by the margo plicatus. Multiple ulcerations (*arrows*) can be seen in the squamous portion of the stomach.

into the splanchnic capillary beds. In addition to sodium-rich fluid losses, increased capillary permeability can lead to loss of albumin and water into the extravascular space, thereby further depleting the plasma volume and the intravascular oncotic pressure. These foals have an immediate requirement of large volumes of isotonic crystalloid fluids and colloids to support their circulating volume.

The goal of intravenous fluid administration is to maintain oxygen delivery to the tissues and oxygen utilization by the tissues. The effectiveness of fluid therapy on oxygen delivery is determined by monitoring for signs of improved cardiac output and perfusion—such as decreasing heart rate, increased pulse pressure, decreased capillary refill time, and increased temperature of extremities.

Isotonic crystalloid solutions include 0.9% NaCl, lactated Ringer's solution, Plasma-lyte, and Normosol R. If the foal is sodium- or chloride-deficient—as occurs with enteritis and uroabdomen—0.9% NaCl is a good choice. For resuscitation purposes, any isotonic crystalloid fluid is appropriate. Fluid rate depends on the goal of therapy. Foals with clinical signs of shock should rapidly receive a shock-dose (40 ml/lb or 90 ml/kg) of prewarmed fluids. Rapid administration of fluids may induce diuresis before saturating the interstitial space; however, this event is inconsequential in treating a foal in hypovolemic shock. Overhydration is not a clinical problem if the heart and kidneys are functioning appropriately and if the foal is not exhibiting signs of severe pulmonary compromise. If the foal is dehydrated, the volume deficit can be estimated by multiplying the foal's weight in kilogram by the percentage of dehydration. The fluid deficit can then be adminis-

tered as a fluid bolus or administered over several hours in addition to the current fluid requirements. The maintenance fluid requirement of a neonatal foal (3-5 ml/kg/hour) is higher than that of an adult and gradually returns to adult values over the first 30 days of life.

Analgesics and Sedatives

Foals may require sedation for various parts of the colic examination. In foals less than 1 month old, intravenous administration of diazepam (0.1 mg/kg) will cause sufficient sedation and recumbency for radiographs and minor procedures. However, it provides no analgesia. If analgesia is needed, butorphanol (0.1-0.2 mg/kg, IV) can be given and will enhance the sedative properties of the diazepam. Xylazine (0.2-0.3 mg/kg, IV or IM) provides analgesia and sedation but produces cardiorespiratory depression. Flunixin meglumine (0.5 mg/kg, q12-24h) is a nonsteroidal antiinflammatory drug that provides excellent visceral analgesia. If gastric ulceration is suspected, administration of nonsteroidal antiinflammatory medications should be avoided.

SURGICAL DECISION MAKING

Determining whether surgical intervention is required can be difficult in foals. The degree of pain is not always helpful in this determination because foals can be in extreme pain with medical diseases such as enterocolitis. However, if the pain is persistent and/or recurs after analgesic medication and medical intervention such as gastric decompression, abdominal exploratory surgery is warranted. Foals with tightly distended small intestine, which indicates mechanical obstruction, are surgical candidates. The presence of nasogastric reflux, abnormal peritoneal fluid, or increasing abdominal distention warrants surgical exploration if the clinical signs cannot be attributed to enteritis. Most meconium impactions will respond to soapy water or acetyl cysteine enemas, oral and intravenous fluid therapy, and small amounts of oral mineral oil. However, if the cardiovascular status of the foal deteriorates and the pain and abdominal distention persist, surgery is indicated.

Distinguishing small or large intestinal mechanical obstruction from infectious enteritis can be difficult. The history of infectious disease on the farm, presence of fever, and abnormal CBC can be helpful but not always diagnostic. Foals have an increased risk of abdominal adhesion formation; consequently, the decision to perform an exploratory celiotomy should only be made after careful evaluation and assessment of diagnostic findings and response to medical therapy. The percentage of foals that survive for long periods after abdominal surgery is less than that of adults in the same situation. However, delaying surgery in foals with surgical lesions can decrease survival as well. Time from diagnosis to surgical correction of strangulating intestinal obstruction significantly affected survival in these foals. Retrospective information indicates that 19% of foals with strangulating abdominal lesions corrected surgically survived more than 2 years, whereas 69% of foals with nonstrangulating lesions survived more than 2 years. Age significantly affected outcome after abdominal surgery in foals. Only 10% of foals less than 14 days old survived after abdominal surgery, whereas 46% of foals between 15 and 150 days old survived—probably because of the large percentage of congenital, nontreatable, abdominal lesions that cause acute abdominal disease in foals less than 2 weeks old.

Supplemental Readings

- Cable CC, Fubini SL, Erb HN et al: Abdominal surgery in foals: a review of 1199 cases (1977-1994). *Equine Vet J* 1997; 29:257-261.
- Cohen ND, Chaffin MK: Intestinal obstruction and other causes of abdominal pain in foals. *Comp Cont Educ* 1994; 16:780-790.
- Fischer AT, Yarbrough TY: Retrograde contrast radiography of the distal portions of the intestinal tract in foals. *J Am Vet Med Assoc* 1995; 207:734-737.
- Robertson SA. Sedation and general anesthesia of the foal. *Equine Vet Educ* 1997; 9:37-44.
- Vatistas NJ, Snyder JR, Wilson WD et al: Surgical treatment for colic in the foal (67 cases): 1980-1992. *Equine Vet J* 1996; 28:139-145.

CHAPTER 12.12

Sedation and General Anesthesia of Foals

SHEILAH ANN ROBERTSON
Gainesville, Florida

Foals must be sedated or anesthetized for a variety of reasons and can be a challenging group of patients. The Confidential Enquiry into Perioperative Equine Fatalities (CEPEF) is a prospective, international, multi-centered study of equine fatalities. Table 12.12-1 shows the mortality rate of foals between birth and 1 year of age. The overall mortality rate is 1.9% with foals younger than 1 month of age having the highest death rate (4.26%). An understanding of the foal's unique physiology and further interpretation of data from the CEPEF allows specific risk factors for this population to be identified.

Neonatal foals (birth to 1 month of age) are physiologically different from adult horses and from other neonates, a fact that makes scaled-down adult anesthetic techniques or extrapolation from other species invalid. To develop an anesthetic plan, the practitioner must have an understanding of equine neonatal physiology and how this physiology influences the action of anesthetic drugs. The final plan will depend on many factors, especially if pre-existing problems such as pneumonia, hypoxemia, dehydration, and hyperkalemia are present.

PHYSIOLOGY

Important cardiovascular parameters are shown in Box 12.12-1. In adult horses, changes in heart rate, stroke volume, or both will alter cardiac output. When cardiac indices are adjusted for metabolic size, foals have a cardiac index (ml/min/kg^{0.75}) at least twice that of adults yet their stroke volume index (ml/beat/kg^{0.75}) is one third less than adults and their cardiac output is primarily rate dependent. This physiology makes foals less able to compensate for the bradycardia caused by α_2 -agonists and hypothermia.

During the first month of life, the foal's mean heart rate is 100 beats per minute (bpm); this rate decreases to an average of 70 beats per minute (bpm) at 2 months and 60 bpm at 3 months. Mean arterial pressure (MAP) values depend on the measurement technique used. With indirect techniques such as ultrasonic Doppler recordings, calculated MAP may be as low as 50 mm Hg in normal 1-day-old foals and rise to 60 to 70 mm Hg at 2 to 3 weeks of age. The MAP in 3-month-old foals is only 75 mm Hg by these techniques, whereas adult values are in the range of 100 to 120 mm Hg. Direct measurement of MAP through an arterial catheter yields consistently higher values, but a steady increase in blood pressure with age is still apparent. Direct MAP should be between 70 and 90 mm Hg

Table 12.12-1
Perioperative Fatality Rate in Different Ages of Foals*

Age (Months)	Fatality Rate (%)
<1	4.26
1-2	1.50
2-5	1.38
6-11	1.54
All (0-12 months)	1.9

*Overall mortality rate is based on 4462 anesthetic records.

BOX 12.12-1

Interdependence of Cardiovascular Parameters

In foals, cardiac output is rate-dependent, and mean arterial pressure is lower because of a lower peripheral resistance, as follows:

$$\text{Cardiac output} = \text{Stroke volume} \times \text{Heart rate}$$

$$\text{MAP} = \text{Cardiac output} \times \text{Total peripheral resistance}$$

MAP, Mean arterial pressure.

from 1 to 10 days of age, increasing to 105 mm Hg in 1-month-old foals. For consistency, blood pressure should be measured by the same technique and with the foal in the same position. The lower systemic blood pressure in foals is a result of a low systemic vascular resistance.

Murmurs are often audible in foals as old as 3 to 5 days and are usually caused by blood flow through a still patent ductus arteriosus, which produces a continuous machinery, or a systolic murmur. Some foals have systolic murmurs until 3 months of age and these are considered benign if they are restricted to the left heart base and do not exceed a grade II murmur (on a scale of I to V). Murmurs can also be the result of high cardiac output, fever and anemia.

On the basis of body weight, foals have a higher minute ventilation (respiratory rate \times tidal volume) than

adult horses, which they maintain with a high respiratory rate. Their tidal volume and values for arterial partial pressure of carbon dioxide (P_{aCO_2}) are similar to adults. Normal respiratory rate is rapid at birth (70 breaths per minute), in the range of 40 to 50 breaths per minute at 1 week of age, then declines toward adult values (15-20) by 1 month of age.

Arterial oxygen tension (P_{aO_2}) in the foal ranges from an average of 65 mm Hg at 1 day of age to 85 mm Hg at 1 week, after which foals gradually attain values in the adult range of 95 to 100 mm Hg. Body position has a significant influence on oxygenation in foals, with values as much as 14 mm Hg higher in standing or sternally positioned animals compared with laterally recumbent foals. Oxygen consumption is 6 to 8 ml/kg/min in the first week of life, a value that is two to three times greater than in adults and is required to meet the foal's high metabolic rate.

Packed cell volume (PCV) at birth averages 43% and falls to approximately 34% during the first 2 weeks of life, most likely as the result of intravascular hemolysis. Hemoglobin values show a parallel decline from a mean of 15.4 gm/dl at birth to 12.6 gm/dl at 2 weeks of age. Foals have total plasma protein values similar to adult horses (60 ± 8 g/L).

The foal's kidneys may be structurally immature but they are functionally mature, with glomerular filtration rates and effective renal plasma flow at 2 days of age similar to that of adults. Blood urea nitrogen values of less than 2 mmol/L (normal mean adult value is 3.5 mmol/L) are normal until the foal is 3 months of age. Foals excrete very dilute urine and have high fluid requirements, drinking as much as 25% of their body weight per day. As a percentage of their body weight foals have greater total body water, blood plasma, and extracellular fluid (ECF) volumes than adults, which may influence the uptake and distribution of anesthetic drugs. In addition, foals require considerable volumes of intravenous (IV) crystalloids to expand or maintain their circulating blood volume.

Indirect evidence suggests that foal's livers also mature early because the pharmacokinetics of chloramphenicol, an antibiotic that undergoes hepatic metabolism, is similar in 1- to 9-day-old foals and adult horses.

The integrity of the blood-brain barrier may influence the response to anesthetic drugs, and clinically foals show more rapid and profound responses to sedative agents, which suggests that their blood-brain barrier is immature.

Foals are susceptible to hypothermia because they lack subcutaneous body fat and have a large surface area to body weight ratio. Compounding this fact are the effects of anesthetic agents that inhibit thermoregulation. Shivering in response to hypothermia increases the already high oxygen requirements of foals by as much as fourfold and could result in hypoxemia. For these reasons, it is important to monitor and maintain body temperature in foals by using circulating water blankets, elevated environmental temperatures, warm IV fluids, and radiant heaters.

SEDATION OF FOALS

Recommended drugs and doses for sedation are shown in Table 12.12-2. Sedation alone may be sufficient for radiography, bandage and cast changes, and joint taps. In foals younger than 4 weeks of age, IV diazepam (0.05-0.25

Table 12.12-2

Recommended Agents for Sedation and Premedication of Foals

Drug	Route	Dose (mg/kg)
acetylpromazine	IM	0.02-0.04
butorphanol	IV, IM	0.1-0.2
diazepam	IV	0.1
xylazine	IV, IM	0.2-0.5*

IV, Intravenous; IM, intramuscular.

*Higher dose can be used when given by the IM route.

mg/kg) causes recumbency and sedation sufficient for many minor procedures; a dose of 0.1 mg/kg is reliable in most situations. Diazepam should be given slowly IV while the foal is gently supported. Within a few minutes the foal will become limp and sedate and can be easily lowered to the ground. Diazepam is not recommended for intramuscular (IM) injection because its uptake by this route is unreliable. Diazepam is less reliable in foals older than 1 month of age, perhaps because of changes in the blood-brain barrier and central nervous system sensitivity. In that age group, xylazine is the first drug of choice for sedation. Acetylpromazine (0.02-0.04 mg/kg IM) will produce mild sedation in foals for several hours. Because diazepam and acetylpromazine provide no analgesia, local anesthetic techniques or butorphanol (0.1-0.2 mg/kg IV, IM) should be added for painful procedures.

Xylazine produces reliable dose-related sedation in foals. No significant differences exist in the cardiopulmonary responses to high doses of the α_2 -agonist xylazine (1.1 mg/kg IV) in healthy 10- and 28-day-old foals, and unlike adults most foals become recumbent. This dose will exert an effect for 60 to 90 minutes. Foal's heart rates fall by approximately 20% to 30%, but blood pressure is well maintained and second-degree atrioventricular block typically seen in adults is rarely seen in foals. The respiratory rhythm of foals is markedly disrupted by xylazine. Upper airway noise indicative of respiratory obstruction occurs for as long as 20 minutes and is likely a result of upper airway collapse caused by pharyngeal muscle relaxation. Despite this effect, healthy foals show no changes in P_{aO_2} or P_{aCO_2} values. In this author's experience, lower doses (0.2-0.3 mg/kg IV) provide adequate sedation and are associated with fewer cardiovascular changes. Xylazine should be avoided in hypovolemic foals and those with respiratory disease, including upper airway obstructions.

Rectal temperature falls significantly after xylazine administration in foals and may be depressed for more than 2 hours after administration. Acetylpromazine can also increase heat loss due to peripheral vasodilation. The foal's temperature should be monitored after sedation and, as previously outlined, efforts should be made to maintain normothermia.

Detomidine (10 to 40 μ g/kg IV) has been studied in foals between 2 weeks and 3 months of age. Unlike their response after receiving xylazine, foals did not become re-

Table 12.12-3

Reasons for Anesthesia and Fatality Rates Associated with Certain Procedures in Foals from Birth to 11 Months

Age (Months)	Colic	Abdominal Noncolic	Fracture	Orthopedic Nonfracture	Urogenital	ENT	Other
<1	8	6	3	47	26	4	5
1-2	5	2	2	68	12	4	6
3-5	5	2	2	41	38	4	8
6-11	6	1	1	32	45	5	10
Fatality rate	12.9*	12.9*	9.1	0.8	1.1	1.5	0.9

ENT, Ear, nose, and throat.

*Fatality rate for all abdominal procedures.

Data are expressed as percentages of foals in the study.

Table 12.12-4

Association between Anesthetic Technique and Risk of Perioperative Fatality

Anesthetic Technique	FATALITY RATE (%)	
	<1 Month n = 680	1-2 Months n = 1131
IV induction, inhalant maintenance	2.7	1.9
Total IV	0	1.2
Total inhalant	6.8	4.4

cumbent. In addition, even low doses of detomidine can be associated with a high incidence of arrhythmias.

GENERAL ANESTHESIA

The CEPEF report provides invaluable insight into both the type of surgery and the anesthetic techniques that are related to high mortality rates in foals (Tables 12.12-3 and 12.12-4). Total inhalational anesthesia was used in 43% of foals less than 1 month old and in 20% of foals between 1 and 2 months. This technique is associated with the highest mortality in both groups compared to less commonly used total intravenous (TIVA) protocols. Overall the highest risk is in foals undergoing abdominal surgery when inhalant agents are used alone.

The preoperative examination must include assessment of heart rate and rhythm, respiratory function (rate and rhythm), color of mucous membranes, hydration status, rectal temperature, and temperament. Further work up and laboratory tests are based on the clinical findings and may include chest radiographs, arterial blood gas, and electrolyte analysis.

The presence of the mare at induction of anesthesia is extremely valuable because her presence usually assures a calm foal. If the foal suckles until anesthesia is administered, adequate blood glucose levels are ensured and re-

gurgitation and vomiting are not a problem. After the foal has been anesthetized, the mare can be housed nearby, but mares often become agitated and may require sedation.

IV catheter placement in healthy foals can be a challenge. A foal may be easy to restrain but when a percutaneous injection is attempted, the same foal may become unruly and be impossible to control. In healthy foals some options exist for IV access. The foal can be sedated with IM xylazine, which facilitates handling. Previous infiltration of the site with 2% lidocaine by using a 25-gauge or 27-gauge needle will decrease the response to placement of a large (usually 14-gauge) catheter. Alternatively the catheter can be placed after induction with IV drugs given "off the needle." Butterfly needles with a length of flexible extension tubing work well in foals. The foal may jump when the needle is placed but is less likely to pull the needle out of the jugular because of the extension tubing.

Injectable Anesthetic Agents**Single Bolus Techniques**

The foal may or may not receive a premedicant agent. If xylazine is used, a dose of 0.25 to 0.4 mg/kg is adequate. Diazepam and/or butorphanol are also suitable premedicant agents and can be given as described for sedation. Ketamine (2 mg/kg) is an excellent and safe induction agent in foals and can be given after xylazine or diazepam.

A mixture of diazepam (0.1 mg/kg) and ketamine (2 mg/kg) can be combined together in the same syringe and given intravenously to induce anesthesia. Approximately 10 to 15 minutes of anesthesia can be expected from this combination. The addition of butorphanol (0.1 mg/kg IV) given as a premedication or at the same time as diazepam and ketamine helps prolong the anesthesia time.

Propofol is a suitable induction agent in foals. It can be given alone, but the amount required is reduced and the quality of anesthesia is improved if the foal is sedated first. A dose of 2 to 3 mg/kg is usually sufficient after xylazine, and this must be given slowly (during 60 seconds) to avoid apnea. Propofol is short acting, and a single bolus, given without prior premedication, may only be effective for 5 minutes but is useful for procedures such as cerebrospinal fluid collection. The prior use of xylazine will

provide approximately 10 minutes of surgical anesthesia. Repeated boluses or infusions (see below) can be used without prolonging the recovery time.

Infusion Techniques

With these techniques, an IV catheter is mandatory and premedication is advisable. A 5% guaifenesin solution can be infused until the foal becomes ataxic, followed by a bolus of ketamine (2 mg/kg). One excellent technique is to add 1 g of ketamine to a 1-L bag of 5% guaifenesin and administer this “to effect.” The guaifenesin/ketamine techniques appear to be intuitively safer because it is the foal that dictates when it has had sufficient anesthetic agent rather than the anesthetist who dictates the dose on the basis of body weight. These techniques are versatile because they can also be used to extend the duration of anesthesia. Oxygen supplementation by facemask, nasal insufflation, or through an endotracheal tube is recommended for all but the shortest of procedures.

Propofol infusions have been used successfully in foals. Xylazine can be followed 5 minutes later by a bolus of propofol (2-3 mg/kg) given during 45 to 60 seconds. Immediately after induction, foals should be intubated and given 100% oxygen. The propofol infusion should be started at approximately 0.3 mg/kg/min and adjusted as needed. Infusion pumps can be used, but the clinician can achieve the same results using IV fluid bags filled with propofol and calculating the “drops per minute” needed. Even after infusions of as long as 2 hours, foals have smooth and rapid recoveries. In one study, cardiopulmonary variables were generally well maintained; there was a mild, but clinically acceptable respiratory acidosis ($P_{aCO_2} < 60$ mm Hg). It must be emphasized that these foals were all given oxygen supplementation. In this author’s clinical experience, hemoglobin saturation declines significantly if foals are allowed to breathe room air during propofol anesthesia. When foals are anesthetized with propofol alone, the level of surgical anesthesia is often inadequate. This technique is useful for short, nonpainful procedures when a rapid smooth recovery is essential. Alternatively, butorphanol can be used or it could be combined with a local anesthetic if the surgical procedure lends itself to local blockade.

Inhalation Agents

The use of inhalant agents as the sole anesthetic technique should be discouraged, because this practice is associated with a high fatality rate when compared with TIVA or induction with injectable agents followed by inhalant agents (see Table 12.12-4). Inhalant agents are potent cardiovascular and respiratory depressants, and when no other agents are used, the amount of inhalant agent required to achieve and maintain anesthesia is greatly increased. The high minute ventilation and cardiac output of foals, combined with a greater perfusion of vessel rich organs (e.g., brain, heart) will likely cause a rapid rise in anesthetic concentration and a quicker onset of anesthesia in foals compared with adults. These rapid changes also make it easy to “overdose” a foal.

Inhalant agents can be used to maintain anesthesia after induction with IV techniques. Halothane, isoflurane, or sevoflurane may be used. No data that compare the safety between these agents are currently available, but a study in

adult horses showed no difference in fatality rate between isoflurane and halothane. Isoflurane may offer some advantages because it results in a more rapid induction and recovery, is less arrhythmogenic, is minimally metabolized, and has a higher therapeutic index. Sevoflurane has recently become available and is licensed for use in horses. Because it is less soluble than isoflurane and halothane, induction and recovery from sevoflurane should be more rapid; however, this has not been substantiated in clinical trials. In 1- to 3-month-old foals, no difference was found in any measured cardiopulmonary variable between those given isoflurane and those receiving sevoflurane.

Once the desired level of anesthesia has been achieved with an inhalant agent, a closed anesthetic system is advisable. With this technique, oxygen is supplied to the circle system at a rate equal to the foal’s metabolic requirements. The pop-off valve is closed and the oxygen flow meter initially is set to provide 6 to 8 ml/kg/min. If the reservoir bag becomes distended, oxygen is being delivered in excess and the flow meter setting should be lowered. Alternatively, if the bag becomes empty, the flow meter setting must be increased to meet the foal’s oxygen requirements. Closed system inhalation techniques are economical and assisted ventilation is simplified because the anesthetist does not have to continually manipulate the pop-off valve. In addition, rebreathing of warmed and humidified gases minimizes heat loss and desiccation of the respiratory passages. An anesthetic breathing circle system designed for small animals or humans will suffice for foals as large as 150 kg if a double CO_2 absorber canister is used. At weights greater than 150 to 200 kg, conventional equipment designed for adult horses is required.

Establishing an Airway before Anesthesia

The technique for nasotracheal intubation can be used when a secure airway is needed before induction with injectable agents—for example in foals with upper airway obstruction or when preoxygenation of the foal is indicated by the presence of pneumonia and hypoxemia. Long (55 cm), cuffed, soft, silicone rubber tubes ranging from 7 to 11 mm internal diameter (30-71 Fr) will be suitable for the smallest to largest of foals. Both the tube and the foal’s nostril are lubricated with lidocaine jelly. The tube is then passed 1 to 2 inches along the ventral meatus, at which time the foal usually struggles a little (Figure 12.12-1). After a pause, an assistant should extend the foal’s head and neck so that the tube can be advanced toward the nasopharynx and into the trachea. When the foal has been successfully intubated, breath sounds are clearly audible and condensation forms on the inside of the tube with each expiration. Once in the trachea, the tube is advanced until the nasotracheal tube connector is flush with the foal’s nostril, at which time the cuff can be inflated. After the tube has been secured with a gauze tie or tape it can be connected to a source of oxygen. Anesthesia may be maintained through the nasotracheal tube. Oral intubation is only necessary if the nasotracheal tube has a very small diameter and provides excessive resistance to breathing.

Supportive Therapy and Monitoring during Anesthesia

The belief that IV dextrose therapy is required in all foals during anesthesia is unwarranted. Normal foals have adult glucose levels (7-8 mmol/L) at less than 12 hours of age, and in the absence of feeding these levels are maintained



Figure 12.12-1 Nasotracheal intubation in a foal. The foal's head and neck are extended while the tube is passed through the ventral meatus.

for at least 2 hours. Foals should only be given supplemental dextrose if blood glucose analyses indicate hypoglycemia. Unnecessary administration may cause a surge of insulin release and rebound hypoglycemia when dextrose is withdrawn. Lactated Ringer's solution should suffice for most routine procedures. The rate of administration depends on blood and fluid losses and clinical assessment but a minimum of 10 ml/kg/hour is recommended.

Pain has negative physiologic and psychologic effects in all species and should always be addressed. It is not unusual for foals to respond to pain more abruptly and profoundly than adults; as mentioned before, their reactions to needle pricks can be dramatic. They may also respond to the initial incision at the start of the procedure even when the depth of anesthesia appears adequate. To reduce the initial response to surgery, local anesthetic blockade is useful and can be achieved with local infiltration of lidocaine or carbocaine. Butorphanol is safe in foals and can be given IV or IM (0.1-0.2 mg/kg). The nonsteroidal anti-inflammatory drugs phenylbutazone, flunixin meglumine, and ketoprofen have been used in foals. Potential side effects of these drugs include gastrointestinal ulceration, nephrotoxicity, and platelet dysfunction; however, these are rarely associated with short-term perioperative use.

Foals require close monitoring during anesthesia. Physical monitoring should include palpation of the peripheral pulse and auscultation of the heart either externally or with an esophageal stethoscope. Blood pressure can be measured directly or indirectly. Blood pressure can be measured indirectly with a cuff placed around the cannon bone. Direct blood pressure monitoring has the disadvantages of being invasive, more technically demanding, and expensive, but is recommended in physiologically compromised foals and when prolonged surgery or substantial blood loss is anticipated. The actual value (mm Hg) at which hypotension is diagnosed will depend on the monitoring technique employed and the age of the foal. Trends in blood pressure values are more informative than single, isolated recordings. A decrease in the level of anesthesia and an increase in the rate of fluid administration should be the first step in management of low blood pres-

sure. If bradycardia is thought to be the cause of the problem, IV glycopyrrolate (0.01 mg/kg) or atropine (0.02 mg/kg) should be given, however, bradycardia caused by hypothermia is often unresponsive to this intervention. Positive inotropes such as dopamine or dobutamine (1-5 µg/kg/min IV) may be necessary to support cardiac output. Electrocardiography is recommended. Arrhythmias are unusual in healthy foals during anesthesia but may occur in foals with uroperitoneum if plasma potassium values are abnormal.

Mucous membrane color is very unreliable for assessing oxygenation status. The most reliable method is analysis of arterial blood samples, but pulse oximetry offers a useful continuous, noninvasive method of monitoring hemoglobin saturation. Adequacy of alveolar ventilation can be monitored continuously and noninvasively by capnography.

General supportive care should include careful positioning, use of protective eye lubricant, and heated water blankets. The immune status of many foals is compromised so invasive techniques such as IV and intraarterial catheterization must be done aseptically. Anesthetic management of septic or metabolically deranged foals differs little from that already outlined, provided that stabilization is accomplished before surgery. Stabilization includes rehydration and, in the case of a ruptured urinary bladder, correction of hyperkalemia.

Foals should be allowed to recover in a dry, warm environment and propped up in sternal recumbency to optimize their PaO_2 . If they shiver, supplemental oxygen should be provided to prevent hypoxemia. When they can be assisted to stand, foals should be reunited with their dam and allowed to suckle as soon as possible to maintain their fluid and caloric intake and to reestablish maternal bonding.

Supplemental Readings

- Baggot JD: Drug therapy in the neonatal foal. *Vet Clin North Am Equine Pract* 1994; 10:87-107.
- Baggot JD, Short CR: Drug disposition in the neonatal animal, with particular reference to the foal. *Equine Vet J* 1984; 16:364-367.
- Carter SW, Robertson SA, Steele CJ et al: Cardiopulmonary effects of xylazine sedation in the foal. *Equine Vet J* 1990; 22:384-388.
- Dunlop CI: Anesthesia and sedation of foals. *Vet Clin North Am Equine Pract* 1994; 10:67-85.
- Johnston GM, Eastman JK, Wood JLN et al: The confidential enquiry into perioperative equine fatalities (CEPEF): mortality results of phases 1 and 2. *Vet Anesth Analg* 2002; 29:159-170.
- Matthews NS, Chaffin MK, Erickson SW et al: Propofol anesthesia for non-surgical procedures of neonatal foals. *Equine Pract* 1995; 17:15-20.
- Pipers FS: Congenital Cardiovascular Disorders. In Robinson NE (ed): *Current Therapy in Equine Medicine*, 3rd edition, pp 408-410. Philadelphia, WB Saunders, 1992.
- Read MR, Read EK, Duke T et al: Cardiopulmonary effects and induction and recovery characteristics of isoflurane and sevoflurane in foals. *J Am Vet Med Assoc* 2002; 221:393-398.
- Stewart JH, Rose RJ, Barko AM: Respiratory studies in foals from birth to seven days old. *Equine Vet J* 1984; 16:323-328.
- Stewart JH, Rose RJ, Barko AM: Response to oxygen administration in foals: effect of age, duration and method of administration on arterial blood gas values. *Equine Vet J* 1984; 16:329-331.

CHAPTER 12.13

Immunodeficiencies of Foals

MELISSA TROGDON HINES

Pullman, Washington

The increased susceptibility of young animals to infection is a well-recognized phenomenon in all species. In foals the period of increased risk appears to extend from the immediate postnatal period for several months. Bacterial infection, particularly gram-negative septicemia, constitutes a major cause of morbidity and mortality in neonates. In foals 2 to 4 months of age, respiratory tract infections are particularly common. Multiple factors probably contribute to the enhanced susceptibility of young animals to infection. Although immunocompetent at birth, neonatal foals are immunologically naïve. In addition, inherent deficits appear to exist in the immature immune system. Furthermore, several specific immunodeficiencies have been recognized in foals that are of significance in individual cases.

IMMUNITY IN NEONATES

Most interest has been focused on development of the specific immune system in foals. However, particularly in naïve foals, nonspecific immune mechanisms undoubtedly play an important role in resistance to infection. On the basis of limited studies in foals and on findings in other species, it appears that many components of the nonspecific immune system, such as complement, neutrophils, and macrophages may be compromised in neonates. For example, evidence exists that foal neutrophils are deficient in phagocytic ability and hydrogen peroxide release, which may predispose to early infection. Also, once gram-negative infection is established in foals, a significant decrease in the neutrophil count usually occurs. Failure of the neutrophil count to subsequently recover has been associated with a grave prognosis. Therefore in an effort to increase neutrophil production and up-regulate function, adjunct treatments such as granulocyte transfusions or administration of granulocyte colony-stimulating factor have been investigated.

The specific immune system of foals is competent at birth, but several studies have documented age-dependent maturational changes in both the systemic and pulmonary immune systems. Functional T lymphocytes are present in the fetus by 100 days of gestational age, although *in vitro* assessment of lymphocyte proliferation suggests that cell-mediated immune function may still be immature at birth. Functional B cells are present by 200 days of gestational age, and equine fetuses are capable of producing specific antibody in response to antigen exposure at this age. Detectable quantities of immunoglobulin M (IgM) are generally found in the fetal circulation before day 200, and are consistently found in the presuckle sera

of normal foals at birth. Wide variation exists in the time of onset of IgG synthesis *in utero*, which may reflect differences in the antigenic stimulation of fetuses. In general, most foals are born with little or no circulating IgG. In immunologically naïve foals, the primary immune response results in detectable serum concentrations of autogenous IgG at approximately 2 weeks of age, with concentrations approaching adult values by 4 months of age. The numbers of circulating B cells may not reach adult values until several weeks of age.

COLOSTRAL IMMUNITY

The diffuse epitheliochorial placentation of the mare does not provide for transplacental transfer of immunoglobulins, and therefore the newborn foal depends on the passive transfer of immunity through the ingestion and absorption of colostrum. A specialized secretion of the mammary gland, colostrum is normally produced under hormonal influences during the last 2 to 4 weeks of gestation. Secretion of colostrum by the equine mammary gland occurs only once during each pregnancy and is short-lived, with colostrum usually being replaced by milk within 12 hours from the time the mammary gland is first suckled by the foal.

Immunoglobulin is the best characterized component of colostrum immunity. The equine mammary gland concentrates immunoglobulins from the circulation. Colostrum contains predominantly IgG and IgG(T), with lower concentrations of IgA and IgM. Specialized epithelial cells in the small intestine are responsible for the nonselective uptake of colostrum immunoglobulins by pinocytosis, the efficiency of which is increased by low-molecular-weight enhancement factors present in the colostrum. The uptake of immunoglobulin from the gastrointestinal (GI) tract declines in time, with the greatest absorption occurring within the first 6 to 8 hours after parturition. Absorption decreases significantly thereafter in most foals regardless of oral intake. By 24 to 36 hours of age, more mature cells unable to take up immunoglobulin replace the specialized enterocytes. The half-life of maternally derived immunoglobulin is 20 to 23 days, and serum concentrations are minimal to absent by 5 to 6 months of age. Because normal foals are producing significant quantities of autogenous immunoglobulin at this age, overall serum immunoglobulin concentrations tend to be lowest in foals at 1 to 2 months of age.

A number of colostrum components other than immunoglobulin contribute to protective immunity in neonates. For example, colostrum is a source of complement and lactoferrin, which enhance host defenses. In ad-

dition, colostrum activates granulocytes, regulates cell-mediated immunity and provides a local protective effect in the gastrointestinal (GI) tract. Some of these effects may be mediated by cytokines present in the colostrum, such as tumor necrosis factor- α , interleukin (IL) 1, IL-2, IL-6 and interferon- γ . These cytokines may influence maturation of the neonatal immune system through their immunomodulatory effects.

FAILURE OF PASSIVE TRANSFER

Failure of passive transfer (FPT), which is the inadequate transfer of colostral immunoglobulin, is the most common immune disorder of foals, with an estimated incidence of between 2.9% and 25%. Although long recognized as a risk factor for sepsis, the actual significance of FPT remains controversial. Although several studies have demonstrated a positive correlation between FPT and the incidence of equine neonatal sepsis, others have failed to confirm such a relationship, and factors other than the amount of immunoglobulin clearly influence the development of infection. These factors include the type of management, environmental conditions, virulence of pathogens, concurrent stress or disease, and the specificity of the antibody. Despite the varying association between FPT and infection, a low serum immunoglobulin concentration is one predisposing factor for infection that can be minimized by management practices. Because of the number of factors that contribute to the occurrence of sepsis, the minimal concentration of immunoglobulin necessary for protection varies with the farm and individual situation. Most normal foals nurse by 2 hours of age and obtain an immunoglobulin concentration of more than 800 mg/dl. Currently, complete FPT is most often defined by serum IgG concentrations of less than 200 mg/dl, partial FPT is defined by serum concentrations of 200 to 800 mg/dl, and concentrations of greater than 800 mg/dl are considered optimal.

Causes of Failure of Passive Transfer

FPT transfer can occur as a result of both maternal and neonatal factors. The major causes include the following:

1. *Loss of colostrum through premature lactation:* Mares that drip milk before parturition have been shown to have lower colostral concentrations of IgG than mares that do not. Although the factors that predispose to this problem are not well understood, premature lactation has been associated with twinning, placentitis, and premature placental separation.
2. *Inadequate immunoglobulin content in the colostrum:* This condition may result either from a failure to produce an adequate volume of colostrum or a failure of the mammary gland to concentrate an adequate amount of IgG. Although variable, the volume of colostrum normally ingested by healthy light-breed foals is approximately 2 to 4 L during the first 12 hours of life. Agalactia or delayed onset of milk production may occur in association with ingestion of endophyte-infected fescue or with serious illness in the mare. Also, because of disruption of the normal sequence of

hormonal changes that occur in late gestation, mares that foal prematurely or in which parturition is induced may not produce enough colostrum of sufficient quality. In general subnormal colostral IgG content (3000 mg/dl) is uncommon in mares that foal at term and do not lactate before parturition. Wide individual variation in colostral immunoglobulin content exists, however, which is partly the result of genetic factors.

3. *Failure to ingest an adequate volume of colostrum in the early postpartum period:* Neonatal weakness or the mare's rejection of the foal are common reasons for inadequate ingestion of colostrum.
4. *Failure to absorb colostrum:* Malabsorption is indicated as a cause of FPT when foals that are known to have ingested an adequate volume of high-quality colostrum have a low serum concentration of immunoglobulin. Although the specialized enterocytes responsible for absorption normally appear early in fetal development, many premature foals have low serum IgG concentrations despite ingestion of colostrum. Because many of these foals have concurrent illnesses, it is unclear whether the low immunoglobulin concentration is the result of malabsorption or differences in the distribution and catabolism of IgG in sick foals. In addition, it has been suggested that elevated concentrations of endogenous or exogenous glucocorticoids may hasten the maturation of the enterocytes and decrease the efficiency of absorption.

Assessment of Passive Transfer of Immunoglobulins

Bacteremia in neonatal foals can develop by 24 hours of age or earlier and makes the early recognition of FPT important. In foals that suckle within 2 hours of birth, serum concentrations of IgG are detectable by 6 hours of age and generally peak by 18 hours. Thus routine evaluation of the IgG concentration in foals should generally be performed at 18 to 24 hours of age when absorption from the intestinal tract is essentially complete. Foals that are considered at high risk for FPT or for infection may be evaluated at 6 to 12 hours of age, allowing for the oral supplementation of colostrum if the concentration of IgG is very low. It is advisable to assess the immunoglobulin status of all sick neonates.

Several tests are currently available for assessing passive transfer. It is important to remember that total protein determination is generally not useful in the foal for evaluating the passive transfer status, because the total protein is influenced by too many factors to accurately estimate the IgG concentration. The most accurate test to determine serum IgG concentration has been single radial immunodiffusion (RID) (Equine RID Kits, VMRD, Pullman, Wash.; Equine-RID, Veterinary Dynamics, Templeton, Calif.), although there is still as high as 20% variability in results. The major disadvantage of this test is that results are not available for 5 to 24 hours. Because rapid therapeutic intervention is important in FPT, numerous field screening tests for FPT have been developed. The zinc sulfate turbidity test, which measures total immunoglobulin based on the formation of a precipitate when immunoglobulin combines with zinc ions, has been widely used in multiple

species. A commercial test kit is available (EQUI-Z, VMRD, Pullman, Wash.), or the reagent may be made. The test requires 1 hour and under some conditions, the concentration of IgG may be overestimated. The enzyme-linked immunosorbent assay (ELISA; Snap Foal IgG Test, IDEXX Laboratories, Westbrook, Me.), designed for the semiquantitative measurement of IgG in equine serum, plasma, or whole blood, uses a color spot with calibration standards that correspond to concentrations of 200, 400, and 800 mg/dl of IgG. The assay is rapid, requires approximately 10 to 15 minutes, and results have correlated well with RID tests. Other available rapid screening tests include the glutaraldehyde clot test (GAMMA-CHECK-E, Veterinary Dynamics, Templeton, Calif.), based on the ability of glutaraldehyde to react with γ -globulin and form a solid clot; and the latex agglutination test (Foalcheck, Centaur, Overland Park, Kan.), which estimates IgG concentration from the degree of agglutination between IgG in serum or blood and latex beads coated with antibody to equine IgG.

Prevention and Treatment of Failure of Passive Transfer

Although many foals with FPT remain healthy, others rapidly develop sepsis. In addition, evidence exists that once sepsis is established it is more difficult to raise serum concentrations of IgG. Therefore prevention of FPT by ensuring adequate consumption of colostrum is optimal. Some studies also suggest that many neonatal infections are acquired soon after birth by the ingestion of bacteria during udder seeking. This finding has led clinicians to recommend improved sanitation, including bathing of the mare and udder, and routine feeding of 100 to 200 ml of colostrum to all foals shortly after birth before they rise in order to minimize chances of sepsis.

When situations do result in diminished passive transfer, no universally accepted recommendations exist for determining which foals require treatment. It is generally recommended that all foals with serum concentrations of IgG less than 400 mg/dl receive treatment, whereas treatment of those with concentrations between 400 and 800 mg/dl is dependent on evaluation of other risk factors, such as environmental conditions and concomitant problems.

Foals that do not suckle or in which FPT is identified at less than 12 hours of age can usually be managed by oral immunoglobulin supplementation. Ideally equine colostrum should be given, with the quantity required depending on the size of the foal, the degree of FPT, the quality of the colostrum and the efficiency of absorption from the intestinal tract, which is usually unknown. Although good-quality colostrum is typically sticky, thick, and yellow, appearance can be misleading. A more accurate assessment of colostral immunoglobulin content can be made by RID, by the glutaraldehyde clot test, or by the measurement of specific gravity by using a colostrometer (GAMMA-CHECK-C, Veterinary Dynamics, Templeton, Calif.; Equine Colostrometer, Jorgensen Laboratories, Loveland, Colo.). The specific gravity of colostrum is directly correlated with the IgG concentration. Acceptable colostrum should have a minimum specific gravity of 1.060 and an IgG concentration of more than 3000 mg/dl. If colostrum from the mare is not available, frozen

colostrum can be given. A colostrum bank can be established by collecting colostrum from mares that die during parturition or lose their foals. Small volumes of high-quality colostrum can be taken from dams of healthy foals without adverse effects on the foal. Approximately 200 to 250 ml of colostrum should be collected within the first few hours after parturition, after the foal has suckled several times, and preferably from the teat opposite that from which the foal first suckles. Ideally, banked colostrum should have a high concentration of IgG (>7000 mg/dl, specific gravity >1.090), and should be free of anti-red blood cell antibodies to avoid neonatal isoerythrolysis. Colostrum can be stored frozen for 18 months without significant loss of IgG, although other components such as complement may be lost. Before administration colostrum should be thawed at room temperature or in warm water. If a microwave is used, it should be set on low power only, since use of high settings can result in denaturation of immunoglobulin. It is recommended that for a 40 to 50 kg foal, 1 to 2 L be administered in 500 ml increments, with 1 hour between feedings. Preferably administration is begun shortly after birth or as soon as possible. This should provide at least 1 gm/kg of immunoglobulin if the colostrum is of sufficient quality. Colostrum can be administered through nasogastric tube or bottle.

Alternative sources of immunoglobulin for oral supplementation do exist if equine colostrum is not available, although most have not been widely used. Bovine colostrum may be safely given to foals and may be of some benefit; however, bovine immunoglobulins appear to have short half-lives in foals and are not specifically directed against equine pathogens. Equine plasma or serum may also be substituted for colostrum and administered orally, but because of their low concentration of immunoglobulin as compared with colostrum, much larger volumes must be given. A number of concentrated equine serum products and lyophilized or concentrated IgG products have been available. While such products may provide adequate immunoglobulin, it is important to remember that for oral administration, most foals deprived of colostrum will require 1 g/kg of IgG, or approximately 40 g for a foal of average size, to consistently raise the IgG concentration from 0 to more than 400 mg/dl. All foals that receive any type of oral supplementation should be tested by 24 hours of age to ensure that absorption of immunoglobulin has been adequate. Testing is especially important if foals are older than 6 hours of age at the time of oral supplementation, because absorption of immunoglobulin may be significantly decreased.

Parenteral treatment is required to correct low immunoglobulin concentrations in foals 12 to 24 hours of age or older, because it is unlikely that sufficient amounts of immunoglobulin will be absorbed from the GI tract. Several equine plasma and serum products are commercially available for the treatment of FPT (Seramune, Sera, Shawnee Mission, Kan; Lake Immunogenics, Ontario, N.Y.; Mg Biologics, Ames, Iowa; Veterinary Dynamics, Templeton, Calif.; Endoserum, Immvac, Columbia, Mo.; VetGen, Ann Arbor, Mich.). These products are convenient, free of alloantibodies and infectious agents, and should provide a known quantity of IgG. Some products originate from horses immunized with endotoxin or with

specific pathogens and may provide increased amounts of specific antibodies, although the degree of additional protection afforded by these products has not been well documented. One disadvantage of commercial products is that they may actually be lacking in antibodies specific for pathogens in the foal's environment. Plasma harvested from a local donor may provide such antibody. Donors should be negative for equine infectious anemia, and should be screened by a blood typing laboratory to establish that they are free of antibodies to equine red blood cells. Also, since plasma separated by sedimentation is commonly contaminated with red blood cells which could sensitize recipients, donors should ideally be negative for the antigens Aa and Qa that are frequently associated with neonatal isoerythrolysis. Because considerable individual variation exists in plasma concentrations of IgG, the IgG concentration in the donor plasma should be measured and should be more than 1200 mg/dl.

The volume of plasma necessary to bring the concentration of IgG into an acceptable range cannot be accurately predicted, because it depends on a number of factors including the severity of the deficiency, the IgG content of the plasma, and the body weight of the foal. Importantly, the presence of existing sepsis can dramatically alter the distribution and catabolism of antibody and increase the volume of plasma required to raise the serum concentration of IgG in the foal. Even in healthy foals in which the amount of plasma administered is carefully calculated, serum IgG concentrations often fail to reach target values. One general guideline for the parenteral administration of immunoglobulin is 200 to 400 mg of IgG per kg of body weight; for plasma of average quality, this is equivalent to approximately 20 to 40 ml/kg. The highest serum concentrations of IgG are attained 1 to 3 hours posttransfusion. To accurately assess the effects of plasma administration and allow for redistribution to extravascular sites, serum IgG concentrations should be measured approximately 24 hours posttransfusion. In a healthy foal of average size, the administration of 20 ml of plasma per kg, or approximately 1 L, typically raises the serum concentration of IgG by a mean of about 200 mg/dl. Therefore in foals that are severely deficient, more than 1 L is usually required. In general 30% of the IgG concentration attained at 24 hours is lost by 7 days. In foals with established infection, repeated plasma transfusion may be necessary to maintain high levels of circulating IgG, although the benefit of such therapy has not been determined. It is also important to remember that high concentrations of immunoglobulin do not preclude the development of infection, particularly with virulent organisms.

Plasma should be administered intravenously, preferably through an inline filter. Frozen plasma should be thawed in a water bath at 39° to 45° C (102°-113° F) and should be warmed to at least room temperature before administration. Recommendations for the rate of plasma administration are largely empiric. The first 50 ml should be given slowly, and the foal should be closely observed for changes in heart rate, respiratory rate or general behavior. Subsequently, plasma can be administered at 20 ml/kg/hr, or approximately 1 L/hr for a 50 kg foal. Administration

should be slower if the foal is oliguric or markedly compromised to avoid overloading the vascular system. If additional plasma is required, the rate of administration is usually decreased, with a second liter given during 2 to 3 hours. Compromised foals may become hypoglycemic if administration of plasma is prolonged and blood glucose concentrations should be monitored in these foals.

Little information is available on the incidence of adverse reactions to plasma transfusions. Tachycardia, tachypnea, restlessness, and muscle fasciculations or shivering occur with some frequency and most often resolve after the rate of administration is decreased. In more severe reactions, marked muscle fasciculations, defecation, hypotension and collapse may be observed. If signs are severe or do not diminish after the rate of administration is slowed the transfusion should be discontinued. Administration of crystalloid fluids may be initiated to maintain the circulatory status. In cases of shock, epinephrine can be given intravenously or subcutaneously at a dose of 0.01 mg/kg in a 1:10,000 dilution (0.1 mg/ml).

OTHER IMMUNOGLOBULIN DEFICIENCIES

Several immunoglobulin deficiencies have been defined in foals in addition to FPT, including transient hypogammaglobulinemia, agammaglobulinemia, and selective IgM deficiency. In these conditions, low serum concentrations of immunoglobulin are typically not recognized until at least 2 months of age if ingestion and absorption of colostrum has occurred. Total lymphocyte counts are generally normal. Although the age of onset and the extent of clinical disease are highly variable, these syndromes are often associated with chronic or recurrent infections that begin when the foal is approximately 2 to 6 months old.

Transient Hypogammaglobulinemia

Transient hypogammaglobulinemia is a rare disorder in which the onset of immunoglobulin production, which normally occurs before birth, is delayed until approximately 3 months of age. Therefore between 2 and 4 months of age, serum concentrations of IgG and IgG(T) are low, and concentrations of IgM and IgA are low to normal. Only rarely reported, the condition may be underdiagnosed because of its transient nature. Although some cases require support in the form of antimicrobial therapy or plasma transfusions, the prognosis for recovery is excellent.

Agammaglobulinemia

Agammaglobulinemia is a rare primary immunodeficiency characterized by the absence of circulating B cells and failure to produce immunoglobulin. Cell-mediated immune function is normal. Actually the disorder is a hypoglobulinemia characterized by low concentrations of IgG and IgG(T) whereas IgM and IgA are generally absent. Recognized in males of several breeds, a mode of inheritance may exist that is similar to X-linked-hypoglobulinemia in humans. Although plasma transfusions and appropriate antimicrobial therapy are beneficial in the short-term, no treatment exists for the condition.

Selective Immunoglobulin M Deficiency

Serum concentrations of IgM are significantly decreased or absent in selective IgM deficiency whereas concentrations of other immunoglobulin classes are normal or increased. Because IgM concentrations may sporadically decrease in seriously ill foals, it is optimal to document that IgM concentrations are persistently depressed rather than to base a diagnosis on a single sample. Although several breeds are affected, the condition has been reported most frequently in Arabians and Quarter Horses. A genetic basis is suspected but not proved. Plasma transfusion provides only temporary benefit, as the plasma concentration of IgM is relatively low and the half-life of transfused IgM is short. The prognosis is generally unfavorable with most cases succumbing by 2 years of age. However, recovery has been reported.

ACQUIRED IMMUNODEFICIENCIES

It is important to remember that secondary or acquired immunodeficiencies also occur, particularly in seriously ill foals, and in many cases the immunosuppression may be transient. Therefore a diagnosis of a primary immunodeficiency should not be made without careful assessment of not only the immune system but also the entire animal. Perinatal infection with equine herpesvirus-1 has been associated with lymphopenia, necrosis and atrophy of lymphoid tissues, and increased susceptibility to infection. Also, a variety of immunologic deficits have been recognized in foals between 2 weeks and 4 months of age with oral candidiasis and bacterial septicemia. Although these immunodeficiencies have been poorly characterized, their prognosis is grave.

SEVERE COMBINED IMMUNODEFICIENCY

Severe combined immunodeficiency (SCID) is a lethal primary immunodeficiency characterized by a failure to produce functional B and T lymphocytes. The majority of affected horses are Arabian or part-Arabian although the disorder has been identified in an Appaloosa. In foals of Arabian breeding, the condition is inherited as an autosomal recessive trait with an incidence of at least 2% to 3%. This percentage is consistent with a carrier prevalence of approximately 25%. Carriers are asymptomatic but can now be detected by genetic testing.

The underlying defect in foals of Arabian breeding with SCID has recently been identified. These foals lack activity of the enzyme deoxyribonucleic acid-dependent protein kinase (DNA-PK) due to a mutation in the gene encoding the catalytic subunit. Without functional DNA-PK, lymphocyte precursors are unable to complete gene rearrangement events that are responsible for the expression of antigen-specific receptors on the cell surface. As a result there is an absence of mature, functional T and B lymphocytes. γ -Interferon, produced by lymphocytes, is also deficient. Components of the innate immune system, including natural killer cells, neutrophils, macrophages and complement, appear to be uninvolved.

Foals with SCID are highly vulnerable to infection as a result of their inability to mount either specific humoral or cell-mediated immune responses. The onset of clinical

disease varies depending on the adequacy of passive transfer and the degree of environmental challenge. Typically affected foals are normal at birth but then begin to acquire infections at 1 to 2 months of age when concentrations of maternal antibody wane. A variety of systemic and localized infections have been recognized, including infections by agents that are rarely seen in normal foals. Recurrent respiratory infections are especially common, and infections caused by adenovirus or *Pneumocystis carinii* are particularly suggestive of SCID.

Currently no specific therapy is recommended for SCID. Supportive treatment such as antibiotics, plasma, and isolation, can prolong the course of disease, but foals usually deteriorate and die by 5 to 6 months of age. Although immunologic reconstitution by bone marrow transplantation from a histocompatible donor is possible, it is not practical.

An accurate diagnosis of SCID is essential both because of the grave prognosis and because both parents are identified as carriers. SCID should be suspected especially in a foal of Arabian breeding with appropriate clinical signs and persistent lymphopenia, as evidenced by lymphocyte counts of less than 1000/ μ l, and most often less than 500/ μ l. It should be remembered that septicemic or other compromised foals, as well as some clinically normal foals, may have low lymphocyte counts, and therefore persistent lymphopenia should be established for a diagnosis of SCID. Other findings consistent with SCID include the absence of IgM in serum collected either presuckle or after 30 days of age when colostral IgM is depleted, and evidence of lymphoid hypoplasia in the thymus, spleen, and lymph nodes on necropsy. The definitive diagnosis of SCID in foals of Arabian breeding is made by genetic testing that confirms that the foal is homozygous for the defective SCID gene. Blood or cheek swabs may be submitted to VetGen (Ann Arbor, Mich.) for DNA testing to determine whether the foal is clear, heterozygous, or homozygous for the gene.

Prevention of SCID relies on the identification of carriers to avoid the production of affected foals. Although carriers can be identified by the production of an affected foal, indicating both parents are carriers, carriers may have many clinically normal offspring because of the autosomal recessive nature of the trait. Therefore all breeding animals should be tested to determine their genotype. Heterozygotes should never be bred to one another. If an owner decides to continue breeding a heterozygote, the animal should be bred only to a homozygous normal individual. All offspring should be tested to determine whether they are clear or heterozygous for the defect (50:50 probability), and heterozygotes should not be used for further breeding.

ANEMIA, IMMUNODEFICIENCY, AND PERIPHERAL GANGLIONOPATHY OF FELL PONIES

A syndrome of severe anemia, immunodeficiency, and peripheral ganglionopathy has recently been reported in Fell ponies. As yet the exact nature of the disorder is unknown, but it is thought to be an intrinsic genetic disorder. No sex predilection exists with the disease. Affected

foals typically show signs of diminished suckling, diarrhea, cough, and chewing motions beginning at approximately 2 to 3 weeks of age. Currently no effective treatment exists for the underlying problem and signs generally progress to death by 4 to 8 weeks of age.

Cryptosporidial enteritis and adenoviral bronchopneumonia, conditions frequently associated with impaired immunity, are commonly identified in foals with this syndrome. However the precise nature of the immunodeficiency is unknown. Although circulating lymphocyte numbers and immunoglobulin concentrations are near normal, affected foals have few secondary lymphoid follicles and lack plasma cells. Circulating lymphocytes show diminished responsiveness to the mitogen concanavalin A.

Supplemental Readings

- LeBlanc MM: Immunologic considerations. In Koterba AM, Drummond WN, Kosch PC (eds): *Equine Clinical Neonatology*, Philadelphia, Lea & Febiger, 1990.
- Perryman LE: Primary immunodeficiencies of horses. *Vet Clin North Am Equine Pract* 2000; 16:105-116.
- Riggs MW: Evaluation of foals for immune deficiency disorders. *Vet Clin North Am Equine Pract* 1987; 3:515-528.
- Robinson JA, Allen GK, Green EM et al: A prospective study of septicaemia in colostrum-deprived foals. *Equine Vet J* 1993; 25:214-219.
- Wiler R, Leber R, Moore BB et al: Equine severe combined immunodeficiency: a defect in V(D)J recombination and DNA-dependent protein kinase activity. *Proceedings of the National Academy of Science (USA)*, pp 11485-11489, 1995.

SECTION XIII

Nutrition

Edited by Dr. Raymond J. Geor

CHAPTER 13.1

Influence of Dietary Energy Sources on Health and Performance

PAT A. HARRIS

Leicestershire, England

DAVID S. KRONFELD

Blacksburg, Virginia

The horse is an increasingly important part of the international leisure industry and a variety of competitions have developed to provide a competitive angle to leisure riding. Critical to feeding for health, vitality, and performance is the appropriate and adequate supply of energy, especially during the training phases. Diets tend to be formulated initially to meet energy needs and then adjusted regarding protein, vitamins, and minerals. However, food calories are not all the same; they differ chemically and these chemical differences affect the mechanism and the efficiency of digestion and metabolism and therefore health and performance.

ENERGY SOURCES

Energy is supplied to the horse via its diet, but fundamentally energy is not a nutrient but rather the capacity to do work. Food energy comprises the potential chemical energy of carbohydrates, fats, and proteins. Part of it can be converted to other body chemicals and mechanical work (useable energy), with the remainder lost as waste energy (mainly in the form of feces, acid, and heat).

Food energy is provided by the following four principal dietary sources:

1. *Hydrolysable carbohydrates*, such as simple sugars and starch, can be digested by mammalian enzymes to hexoses, which are absorbed from the small intestine (SI) or if they "escape" digestion in the SI they are fermented rapidly in the hindgut.
2. *Fermentable carbohydrates* are components of dietary fiber, such as cellulose, pectins, and hemicelluloses. These are not digestible by mammalian enzymes but can be fermented by the microorganisms located predominantly in the hindgut. Speed of fermentation and the site of fermentation may play an important role in the energy value to the horse.
3. *Oils and fats* are not part of the horse's "evolutionary traditional" diet containing relatively low concentrations of oils. However, horses in general appear to be able to digest and use up to 20% of their diet as oil if suitably introduced.
4. *Proteins* are not a nutritionally preferred option as an energy source. These nitrogen-containing nutrients are converted inefficiently to useable energy with proportionally higher amounts of waste energy in the form of heat, acid, and nitrogen. The nitrogen is removed as urea resulting in increased water requirements and potentially increased levels of irritant ammonia in the stable.

Different feeds and feedstuffs contain varying amounts of potential chemical energy from these four main energy sources. The efficiency of their conversion to useable energy, such as kinetic energy or work, differs. Individual variability also occurs in the capacity to digest and use the energy, which means that the amount of energy that different feeds ultimately provide to each horse obviously varies. However, in general terms cereals provide more useable energy (and less waste heat) than does hay, which

in turn provides more than twice the net or useable energy than straw. This means that under cold conditions, feeding increased levels of forages can be beneficial for thermoregulation, but in hot and humid conditions high forage-based diets can impose additional thermal stresses, especially on performance horses.

In France and other parts of Europe the energy content of feeds and requirements are evaluated using a net energy system. However, the usual energy currency for horses in much of Europe and America is based on digestible energy (DE, kcal per gram of substance or Mcal per kg or MJ per kg where 1 Mcal = ~4.184 MJ), which is calculated from the gross feed energy or intake energy and the digestibility of the feedstuff (an efficiency factor).

Currently lacking is a good means of accurately and easily predicting the energy content of different feeds because typical proximate analysis, based on fat, fiber, and protein content, lumps together substances that have similar chemical characteristics. The usually unstated assumption, that these substances also have similar digestive and metabolic fates, has serious limitations. For example, sugar beet pulp (SBP) may provide more energy to the horse than its traditional crude fiber, protein, and fat analysis would suggest (approximately 20% more). This is in part because sugar beet pulp contains major fractions of pectins, arabinans, and galactans lost during the crude fiber analysis, yet these carbohydrates can be fermented and thereby used by the horse. In addition, the fiber, or more specifically the nonstarch polysaccharide (NSP), in beet pulp is highly digestible over the total tract with a significant proportion being degraded (around 16.5% of unmolassed SBP NSP) in the small intestine during transit to the hindgut. The various digestibility studies suggest that SBP is well fermented in the horse and this degradation occurs to a large extent within the time period that such a feedstuff would remain within the gut. This helps explain why sugar beet pulp and a similar feedstuff, soybean hulls, are increasingly being used as fiber-based energy sources in modern horse feeds.

This inconsistency in being able to predict the energy content of feedstuffs complicates any understanding of equine nutrition based on proximate analysis and undermines the scientific formulation of horse feeds. However, an appreciation is growing of how to better characterize the fermentable carbohydrate content of horse feeds using various analytic techniques. Table 13.1-1 shows these authors' current approximations for determining the DE values for horse feedstuffs.

ENERGY REQUIREMENTS

Optimal feeding of horses uses both art and science. The science provides the information about the digestive and metabolic processes, the nutrient requirements, and the principles behind feeding practices. The art is the ability to convert this theory into practice for the individual horse, addressing its needs, likes, and dislikes.

Adult horses tend to be fed initially for energy and then the diet is balanced for protein, vitamins, and minerals. The first stage of formulating any diet is to determine energy requirements, noting that mean DE requirements for horses of specified body weight (BW) and age given in the

various nutrition texts are only an initial guide as individual variation is 10% to 20%. In addition, horses have a finite appetite, which influences what they can be fed to meet their energy requirements. Daily feed intakes tend to range between 1.5% and 3.0% of BW on an *as fed* basis for most adult horses, although nursing and weanling foals may eat significantly more. A typical adult horse at rest requires approximately 3.1 to 3.6 Mcal DE (13 to 15 MJ DE) per 100 kg BW and needs to eat around 1.5% to 2.0% of its BW in dry matter (depending on energy content) to meet demands. If the energy content of the feed is high or the animal is metabolically efficient (an "easy keeper"), it may be able to meet energy needs at a lower level of feed intake. However, such an intake may not satisfy its psychologic needs (time spent chewing), in which case the diet, for example, could be bulked out with a lower energy feed such as mature hay or chaff.

Inadequate energy intake leads to losses of BW in this order: gut fill (hours and days), water and electrolytes (hours and days), fat (days and weeks), protein (weeks and months), and bone minerals (months and years). The first four of these losses can be assessed readily by physical examination. This means that the feed intake to achieve a desired BW and degree of fatness or body condition score (BCS) for a horse should be decided precisely for each individual by weekly adjustments based on BW and BCS. The ancient adage—the *eye of the farmer fattens the ox*—is a better guide than any table or equation in a book. Fundamentally if a horse is fed too little energy for its needs it tends to become dull and lethargic and can lose weight and/or become clinically ill. If a horse is fed too much energy or inappropriate energy it may become hyperactive and may gain weight and/or become ill.

The second stage in formulating a diet is to check the protein: energy ratio, the first concept of the balance of a ration. The amounts recommended for maintenance and physical conditioning are about 40 g per Mcal DE (9.6 g per MJ DE) per day (10% of DE). Higher amounts are needed for young growing animals, as well as pregnant and lactating mares. Under active study are protein quantity and quality for intense exercise and old age. In these authors' experience, old horses losing BW and BCS amidst an abundance of low-protein forage (winter pasture, mature hay) usually respond to an increase in protein intake, for example, provision of about 10 lb of alfalfa hay or about 7 lb of 16% CP concentrate. Although essential amino and fatty acids and vitamins and minerals do not change the energy potential of a diet, any deficiency, excess, or imbalance can reduce the efficiency of energy utilization.

FEEDING FOR ENERGY

Forages

The horse evolved as a grazing animal, which escaped predators by flight and was adapted to an almost constant supply of forage from grazing and browsing plants. Suitable forage is the safest feed to give horses and occupies their time in chewing and helps maintain a healthy gastrointestinal tract. Forages should be the foundation of all diets. Some horses and ponies may not require any other food. Forages with higher energy levels and greater

Table 13.1-1

Approximate Digestible Energy Values of a Feed Estimated from the Content of Its Various Energy Sources

Energy Source	Gross Energy	Digestibility	Digestible Energy	Comments	
Carbohydrates					
Hydrolysable					
Sugar and starch determinations	4.2 kcal/g (17.6 kJ/g)	Digestion is 100% for hydrolysable carbohydrates but varies considerably for fiber fractions from 35% to 60%.	4 kcal/g	Currently available carbohydrate fractions relate better to plant anatomy and chemistry than to equine digestion and metabolism. Required for the horse are fractions that relate to speed of fermentation—that is, rapid to lactate and propionate and slow to acetate and butyrate. Proximate carbohydrate analysis also should include lignin (a propane polymer that is not a carbohydrate) because the rate of fermentation of hemicellulose and cellulose is affected by their lignification.	
Fermentable					
a. Rapidly fermentable— Estimated by: (NFE-NSC)	4.2 kcal/g (17.6 kJ/g)		a. 2.5 kcal/g		
b. Moderately fermentable— Estimated by (NDF-ADF)			b. 2.0 kcal/g		
c. Slowly fermentable— Estimated by ADF			c. 1.5 kcal/g		
Fats and Oils					
	9.3 to 9.7 kcal/g	The EE of forages contains much indigestible wax and pigment, so that the overall digestibility is about 55%.	~5.3 kcal/g (22 kJ/g)	In a set of 18 trials the true digestibility of added corn oil was 100% up to 230 g/kg of fat in feed, and endogenous fecal fat was 54 g/day, which accounted for the 95% apparent digestibility. Accommodation to increased dietary fat was allowed in these experiments, and the lipolytic capacity of the small intestine may adapt to an increased load of fat over a period of days or a few weeks.	
		Added vegetable oils and animal tallow are about 99% triglycerides, with an apparent digestibility of 95%.	9.0 kcal/g (38 kJ/g)		
		Feed fats and oils have a lower content of triglyceride, which is reflected in a lower digestibility.	~8.0 kcal/g		
Protein					
	5.3 kcal/g	The digestibility of true protein probably exceeds 90%, but a representative value for CP in many common horse feeds is about 70% to 75%.	3.8 kcal/g (16 kJ/g)	Crude protein (CP) is estimated as nitrogen multiplied by an average factor (6.25). This calculation overestimates true protein, because of non-protein N such as urea, purines, and pyrimidines. Some protein is denatured to indigestible products during cooking and processing, which remain represented in CP. Protein digestible energy is used efficiently for anabolism or build up of body substances but not for work, because using amino acids for work wastes urea.	

NFE, Nitrogen free extract; NSC, nonstructural carbohydrates; NDF, neutral detergent fiber; ADF, acid detergent fiber; EE, ether extract.

digestibilities should be considered, especially for those animals in competitive work. Those in little or no work or that are "easy keepers" may benefit from being fed roughages of lower energy content. Alternative energy sources should be considered only when the horse's condition and/or energy requirements cannot be met by forage alone (sometimes small amounts of grain or other concentrates also may be needed to carry supplemental protein or minerals to balance the ration) or a clinical reason exists why high forage-based diets are not desirable. For the majority of horses, at least 50% of their diet on a dry matter (DM) basis should be suitable forage (around 1 kg per 100 kg BW). Even fit, intensively working horses should be fed 35% to 50% of their DM intake as forage. Exact amounts vary according to the type (content of various fibers) and quality of the forage.

Pastures and conserved forages differ considerably in quality and nutrient content based on the plant species present, the geographic region, climate, management, and harvesting methods. Most forages, when fed alone, do not support the nutritional requirements of horses throughout the whole year, especially for horses that are growing or in work. An appropriate vitamin and mineral mix alone may be satisfactory for many horses at rest and, depending on the pasture, for those in light or moderate work. In addition, supplemental energy sources are likely to be required for the young growing animal, the pregnant and lactating mare and for those in hard work.

Ponies, especially fat and/or pregnant ones, have an increased risk of developing hyperlipemia. They should not be starved abruptly to reduce their body weight or prevented from eating for prolonged periods. Reducing the diet to a half maintenance level is safer than completely starving a pony for weight loss purposes. Wherever appropriate, the diet can be formulated to satisfy near appetite levels by the addition of low energy forages. However, poorly digested, highly silicated forages such as straw may increase the risk of impaction.

Energy Concentrates

Traditional energy concentrates are cereal grains (containing abundant starch, which is digested primarily in the small intestine), and molasses (sugars). The upper part of the gastrointestinal tract has a relatively small capacity, and the horse has digestive and metabolic limitations to high grain, starch-, and sugar-based diets. Large grain meals may overwhelm the digestive capacity of the stomach and small intestine, which leads to the rapid fermentation of the grain carbohydrate in the hindgut and a number of potential clinical consequences. This has led to the increasing use of non-sugar- and starch-based energy sources, especially alternative fiber sources such as sugar beet pulp and soybean hulls, which provide more energy than typical forages (as discussed above). In addition, adding sugar beet pulp to the diet may increase the nutrient value of concurrently fed hay, especially hay of low protein content. Sugar beet pulp shreds can be obtained in molassed and unmolassed forms, which obviously affect the sugar content of the feedstuff. In addition, it is usually recommended that sugar beet pulp, particularly the unmolassed form, is soaked thoroughly before feeding.

Most forage-based diets and those based on grains, fat-extracted oil seed meals and hays contain between 2% and 5% oil. Recently use of supplemental vegetable oil in horse diets has increased. Initially, this was common only in the endurance discipline, but it is being recommended increasingly for many performance horses. Vegetable oils have about 2.5 times as much DE as maize or corn and 3 times as much as oats. Other more exotic concentrated energy sources tend to combine the provision of both oil and fiber, for example, rice bran (18% to 22% fat with variable starch content and an imbalanced calcium to phosphorus ratio) and copra meal (e.g., about 8% to 9% fat, 12% to 16% crude fiber, a low starch content <2%, a high crude protein content of about 22% but a low lysine content, about 6 g per kg).

Feeding these concentrated energy sources effectively means that the horse may take in more energy even if its appetite decreases. This boost can be valuable especially in the nutritional support of sick horses. High-fat feeds also may benefit the equine athlete when combined with training over several weeks or months, a process known as *fat adaptation* (discussed below). Practical problems with high-fat feeds are potential poor acceptance and the need to introduce them gradually to allow the digestive system to adapt, which takes up to 3 weeks.

INFLUENCE OF ENERGY SOURCE ON HEALTH

Public health effects of carbohydrates and fats have been contentious over the last 50 years. Low-fat diets touted for prevention of heart disease in humans have, in effect, been abundant in sugar and starch. These high-carbohydrate diets have been associated with insulin resistance and an associated group of diseases known collectively as *syndrome X*. The group includes non-insulin-dependent diabetes mellitus (NIDDM; type 2 diabetes), hypertension, atheromatous heart disease, cystic ovaries in women, and oxidative stress. Similarly, feeding sugar and starch to horses as large grain-based meals has been implicated in a group of disorders and diseases that, for convenience, may be known collectively as *equine grain associated diseases* (EGAD). Similar conditions are being seen with the intake of lush pastures containing large amounts of rapidly fermentable nutrients. Some of these conditions are digestive in nature, such as osmotic diarrhea, cecal distention colic, acidic enteritis, laminitis, and perhaps gastric ulcers. Others are metabolic disorders involving insulin resistance, resembling human syndrome X. This equine syndrome X probably includes some forms of developmental orthopedic disease (DOD), the equine rhabdomyolysis syndrome (ERS), and laminitis.

The horse evolved as a nibbling grazer and developed a digestive tract that favors fermentation of forages in the large bowel relative to hydrolytic digestion of grains in the small intestine. When the limited hydrolytic capacity of the equine small intestine is surpassed, the soluble carbohydrates that escape hydrolysis are fermented rapidly in the large bowel, predominantly to lactic acid, which is absorbed poorly and accumulates in the lumen. Lactate attracts water, setting the stage for osmotic diarrhea and cecal distention colic. Rapid fermentation also yields

much gas, which may contribute to cecal distention. Accumulating lactic acid lowers the pH below a critical level, lysing those bacteria that cannot survive at this pH, releasing endotoxins and other unwanted compounds into the hindgut. These may be absorbed into the blood and have further effects. The blood flow to the feet, for example, may be particularly sensitive to some of these factors, the result being the development of laminitis. The change in hindgut conditions may damage the mucosa and if severe allow bacteria to adhere and penetrate, contributing to colitis and diarrhea.

Turning horses and ponies out onto lush pastures in the spring and autumn is another common triggering factor for the development of laminitis. High levels of water-soluble carbohydrates, including fructans, may be involved in this process. The horse is believed to not have the necessary enzymes to digest fructans directly within the small intestine. Fructans therefore pass into the hindgut, where they are fermented to lactic acid, in a similar manner to starch that escapes digestion in the small intestine.

Feeding a grain meal raises plasma concentrations of glucose and insulin for 4 to 6 hours. These responses are reduced greatly by replacing starch and sugar with fat and fiber. Feeding two-grain meals a day sets up a feeding-fasting cycle of metabolites and hormones, which is alien to the nutritional heritage of the horse. Elements in the feeding-fasting cycle have been suggested to contribute to developmental orthopedic disease, such as fluctuations in glucose and insulin, thyroid hormones, growth hormone, and insulin-like growth factor-1.

Although no single procedure or set of procedures can guarantee against further episodes of ERS, appropriate management procedures and nutrition of susceptible animals (in particular replacing starch and sugar with fat and fiber) may help to reduce the likelihood or frequency of future episodes.

In contrast to rapid fermentation of soluble carbohydrates, heavily lignified cellulose in mature hay or straw is fermented slowly. It may accumulate, most commonly in the large colon, and contribute to impaction colic, an example of a non-EGAD condition that may be associated with the nature of the energy sources fed.

In conclusion, the indications for changing the nature or type of the energy sources in equine diets are therefore to reduce the risk of disease and to improve athletic performance. Claims that energy sources influence health and disease risks are based on epidemiologic studies, clinical trials, and physiologic studies (Box 13.1-1).

ENERGY SOURCES AND PERFORMANCE

Athletic performance may be improved by fat adaptation, a set of physiologic responses to feeding a higher fat diet during physical conditioning (several weeks or months are required for full adaptation). These adaptations may include the following:

- Increased mobilization of free fatty acids (FFA) and increased speed of mobilization plus increased speed of uptake of FFA into muscle
- Less production of waste heat and acid, factors that contribute to fatigue

BOX 13.1-1

Indications for the Substitution of Fat and Fiber for Starch and Sugar*

Colic—cecal distention: E, P
 Enteritis: E, P
 Diarrhea—osmotic: P
 Laminitis, founder: E, P, T
 Gastric ulcers: E, P
 Equine rhabdomyolysis syndrome (some forms): E, P, T
 Osteochondrosis (some forms): P
 Growth spurts and slumps: E, P, T

*On the basis of epidemiologic evidence (E), physiologic studies (P), or clinical trials (T).

- A glycogen-sparing effect so that fatigue is delayed and performance improved, which is especially important in endurance activities

In addition, faster times have been recorded on the race-track (1 mile distance), mainly as a result of a faster first furlong. Metabolic studies reveal moderated plasma lactate increases during slow work but augmented lactate responses to hard work. These findings indicate improved metabolic regulation in fat-adapted horses, which can augment the high-power source (anaerobic glycogen breakdown to lactate) when needed for sprinting. These findings suggest increased high-intensity exercise capacity with fat adaptation.

Replacing forage with cereals and/or fat decreases the amount of feed the animal must eat to meet energy needs (important because horses have a finite appetite). In addition, the attendant reduction in gut ballast or fill (and BW) may provide a biomechanical advantage during exercise. However, this should not be taken to extremes because an adequate fiber intake is needed to relieve boredom, assist with fluid dynamics, and maintain a healthy hindgut.

Using vegetable oil as a concentrated energy source has other potential advantages:

- More fiber often can be fed with less cereals or hydrolysable starch while maintaining the desired energy intake. This in turn helps to maintain the microfloral population in the hindgut and prevent the overproduction of lactic acid, which could lead to digestive and other metabolic disturbances.
- An oil-supplemented diet also may have behavioral advantages over high cereal and starch diets. Decreased spontaneous activity and reactivity has been reported in fat-adapted horses and a calmer disposition is also evident in foals and yearlings fed fat- and fiber-based (rather than the more traditional starch- and sugar-based) feeds.
- Oil in the diet is converted more efficiently to useable energy than are feeds such as hay and cereals. This may help to reduce the heat load on the horse. This may be particularly useful when competing under hot

and humid conditions. A reduction in heat load also should decrease the water requirement.

- Oil-supplemented diets reduce fecal output, fecal water, and bowel ballast.
- Additional oil may benefit skin and hoof appearance, but exact requirements of fatty acids are unknown.
- Weanlings and yearlings fed grains and sweet feeds exhibit slumps and spurts of growth rate and show pronounced glucose and insulin fluctuations associated with meal feeding (which may increase the risk of DOD). These fluctuations may be smoothed out in horses fed fat-and-fiber feeds.

FEEDING RECOMMENDATIONS

Cereals and Starches

The size of grain-based meals should be limited. However, guidelines can depend on the type of starch being fed and how it is being fed. Researchers in German and Texas have recommended meal limits of 2 and 4 g starch per kg BW respectively, and these correspond to meals of no more than 2.5 or 5 lb of grain-based concentrate for an 1100-lb (500-kg) horse. Several studies have shown profound digestive, circulatory, hormonal, and metabolic responses to grain meals of about 4 lb and exaggeration of these responses is expected with larger meals. Recent work suggested that although at 3 g starch per kg BW all the oat starch was digested in the small intestine, 20% of the barley starch and 34% of the cornstarch escaped prececal digestion and reached the large intestine. Cooking or micronizing cereals such as corn and barley improve their prececal digestibility. When corn or barley is included in equine rations, these grains therefore should be heat-treated. A current recommendation is to feed less than 500 g per 100 kg BW per concentrate meal and less than 400 g per 100 kg per meal for straight cereal grains (2 kg or less per meal for a 500-kg horse). When large intakes of grain are required it is advisable to feed smaller, more frequent concentrate or cereal-based meals rather than an occasional large meal. Feeding by weight rather than by volume (scoop, bucket, etc.) also is important. Oats, for example, weigh 20% to 40% less for a given volume than corn.

The microbial population of the hindgut becomes adapted, usually in a few days, to the type of feed provided. Rapid changes in *any diet* may result in marked fluctuations in this microbial population, which can result in imbalances and in certain circumstances digestive disturbances such as diarrhea or colic. Therefore the amount rather than type of feed should be varied when possible. However, sudden changes in the amount of concentrates fed (especially increases) are particularly likely to produce problems and therefore any changes should be made gradually. Small changes should be made in a stepwise manner over 3 to 5 days. More major changes should be accomplished over a 2- to 3-week period. Even in a fully grain-adapted horse the grain (concentrate) should never be increased by more than 0.5 kg per day (for a 500-kg horse).

For "hard keeper" horses that have difficulty maintaining condition (with no suspicion of ill health) consider the following:

- Increasing the number of meals per day (while keeping down the size of each meal)
- Changing to a feed with higher energy content, or substituting some of the forage intake for a higher energy feed providing storage or including alternative energy sources such as sugar beet pulp or soya hulls
- Adding additional oil

Additional Oil

Common equine feedstuffs contain only 2% to 4% fat. Performance products are fortified with fat, usually vegetable oil, to contain from about 6% up to 14% fat (as fed) by weight (approximately 9% to around 30% of DE). As the energy density increases, feeding rates may need to be decreased to avoid gain of body condition. Reduced concentrate intake allows more forage (fiber) to be fed. The overall effect is replacement of starch and sugar by fiber in addition to fat. The most common substitution is fiber (2 parts) and fat (1 part) for starch and sugar (3 parts).

The horse's hydrolytic capacity for fat seems to be adaptable (unlike starch), but this accommodation takes time. Therefore any additional oil or oil rich feed should be introduced gradually. In fact horses have been shown to be able to digest and use up to 20% or more of the diet (by weight) as oil when well adapted, which takes 2 to 3 weeks of gradual introduction of the oil. Acceptance of high-fat feeds or added fats and oils is often difficult. Preference tests on numerous fats have demonstrated that corn oil is in general the best accepted, although this varies with the individual, the type of oil being used, and how it has been processed. Animal tallow tends to be the least palatable and are not recommended. Common observations suggest that certain rice brans are readily accepted. Rejection of oils or high oil diets may be immediate or delayed a few weeks or months.

Several trials have confirmed the value of incorporating around 12% oil by weight in a complete and balanced feed. However, adding oil to existing feed has the potential to create multiple imbalances and therefore could be considered less safe than feeding a diet in which the oil has been balanced in relation to all of the essential nutrients in the feed. Therefore when adding oil to diets, using less than the 12% suggested above is prudent. Levels of 5% to 8% in the total diet are more common in feeds for the competition horse and it has been recommended to feed a maximum of 100 g of oil per 100 kg BW per day. The majority of animals (500 kg BW) can be supplemented up to 16 fl oz per day (approximately 400 g) in divided doses without any problems, provided that the oil has been introduced gradually, the extra energy is required, and the oil is not rancid.

When adding supplemental oil to the diet, for an 1100-lb or 500-kg horse, 2 to 4 tablespoons (30 to 60 ml) or $\frac{1}{4}$ cup per day can suffice as an initial dose. (A standard breakfast cup contains around 8 fluid ounces or approximately 250 ml of water and holds approximately 200 g of corn oil. This equates to 1.6 Mcal [6.7 MJ], or one tenth of the approximately 16 Mcal DE maintenance requirement of a 500-kg [1100-lb] horse). Over a 2- to 3-week period, the amount of oil added can be increased up to 1 cup (approximately 200 g) twice a day if required. In some

circumstances, providing the diet is properly balanced, horses can be fed up to two cups twice a day if even more energy is required. For hypometabolic sick horses, a similar or more gradual approach is prudent. For the hypermetabolic sick horse, however, more aggressive nutrition support may be needed and tolerated (see Chapter 13.2: "Clinical Assessment of Nutritional Status and Enteral Support in the Acutely Ill Horse"), taking special care in both cases to ensure the optimal supportive vitamin and mineral intake.

Alternatively oil-rich feedstuffs such as certain seeds, copra meal, and rice bran can be used, allowing for any consequent nutrient imbalances. Or a manufactured, balanced high-oil feed, which has been designed to complement the forage source, can be fed. To promote acceptance of such a high oil feed it should initially be mixed with the horse's customary feed.

Pure fats and oils contain no additional vitamins or minerals. Therefore if the diet does not provide adequate vitamin and mineral fortification, an appropriate additional mix may be needed. In addition, extra vitamin E is recommended to maintain antioxidant status (an additional, on top of a basal level of 160 IU per kg DM intake, 100 IU vitamin E per 100 ml added oil is suggested unless the oil being used is rich in available antioxidants).

FEED FORMULATION

Obviously diets for horses should be adequate and balanced with respect to their energy, protein, vitamin, and mineral contents. The commonly used reference book *NRC National Research Council's Nutrient Requirements of Horses* presents mean minimum requirements. Consequently, the NRC for horses should not be used like the NRC requirements for production animals (which are optimal for specified levels of production) when formulating horse feeds.

The balance of a ration usually emphasizes the ratios of essential nutrients to energy. However, as outlined above, other balances relating to the energy sources in the diet should be considered when formulating the op-

timal diet for an individual under specific circumstances, for example:

1. Sufficient hydrolysable carbohydrate to help maintain glycogen levels, and help provide a sufficiently energy dense ration without overloading the hydrolytic, digestive capacity of the horse
2. Adequate fat/oil to maintain the required energy density of the ration without adversely affecting palatability and gastrointestinal function
3. Heat production, which is minimized or maximized according to requirements
4. Sufficient fiber to maintain normal gut and digestive function and limit behavioral disturbances

In conclusion, with respect to dietary energy the amount and the balance between the various energy sources help promote required athletic performance while minimizing the risk of clinical disorders.

Supplemental Readings

- Clarke LL, Roberts MC, Argenzio RA: Feeding and digestive problems in horses: physiologic responses to a concentrated meal. *Vet Clin North Am Equine Pract* 1990; 6:433-450.
- Cohen ND: Epidemiology of colic. *Vet Clin North Am Equine Pract* 1997; 13:191-201.
- Cuddeford D: Starch digestion in the horse. In Pagan JD, Geor RJ (eds): *Advances in Equine Nutrition II*, pp 95-103, Nottingham, United Kingdom, Nottingham University Press, 2001.
- Davidson N, Harris PA: Nutrition and welfare. In Warren N (ed): *The Welfare of Horses*, pp 45-76, Dordrecht, Netherlands, Kluwer Academic.
- Harris PA: Energy requirements of the exercising horse. *Ann Rev Nutr* 1997; 17:185-210.
- Kronfeld DS: Clinical assessment of nutritional status of the horse. In Watson TDG (ed): *Metabolic and Endocrine Problems of the Horse*, pp 185-217, London, WB Saunders, 1998.
- NRC: *Nutrient Requirements of Horses*, 5th edition, Washington, DC, National Academy Press, 1989.
- Valentine BA, Van Saun RJ, Thompson KN et al: Role of dietary carbohydrate and fat in horses with equine polysaccharide storage myopathy. *J Am Vet Med Assoc* 2001; 219:1537-1544.

CHAPTER 13.2

Clinical Assessment of Nutritional Status and Enteral Feeding in the Acutely Ill Horse

ANDREA J. FASCETTI
MERI STRATTON-PHELPS
Davis, California

Malnutrition has been clearly linked to increased morbidity and mortality rates in humans, and it is believed to have a similar effect on veterinary patients. Although never quantified, malnutrition appears to be more common in veterinary patients than previously recognized. Defined as *abnormal nutrition*, malnutrition can be the result of an unbalanced intake of protein and/or calories to support tissue metabolism and has the potential to undermine proper medical or surgical therapeutic management. A reduction in food intake is likely to result in a deficiency of both protein and calories in many hospitalized patients. Horses resting in a stall may appear to require little or no nutrition when, in fact, their needs are significant. The consequences of malnutrition include altered gastrointestinal function, decreased immunocompetence, poor wound healing, and alterations in intermediary drug metabolism.

PATIENT ASSESSMENT: DIET HISTORY

The goal of nutritional assessment is to establish a horse's needs and feeding goals in light of its physiologic or disease condition. The horse's nutrient needs are the benchmark for assessment of the animal's diet. Assessment of a horse to determine its nutritional status should include the following: a thorough review of the patient's history and medical record, a complete physical examination, laboratory and other diagnostic tests; and an estimation of the key nutritional goals on the basis of the patient's physiologic state and medical condition.

Every animal's medical record should include a complete diet history in conjunction with the background medical information obtained during the examination. Questions should be asked about the weight of the animal and whether or not the body condition of the animal has changed recently. Therapies that may affect appetite, nutrient metabolism, or both should be entered into the record. An adequate diet history should include a list of all ration and diet components, the amount of feed offered and consumed, the feeding schedule, the method of feed delivery, and identification of the person who most often feeds the horse. The feeding environment of the horse should also be evaluated to determine whether competition with other horses for food is present, or if the an-

imal has repeated exposure to debris such as wire from tires or bailing twine that could serve as a nidus in the formation of enteroliths. Horses fed on a dirt or sand surface can ingest high volumes of sand that could result in a large colon impaction or sand colic. An evaluation of the pasture where the horse is maintained may be required if the patient has not received proper nutrition, and has instead consumed the native pasture, which could include toxic plants (e.g., *Senecio* sp., fiddleneck, yellow star thistle). If the diet is changed frequently, the practitioner should inquire as to the cause for the frequent alterations, and the result of the diet changes on the horse. Intake of treats, mineral blocks, and nutritional supplements, as well as water consumption, should also be recorded. Dietary supplements should be carefully evaluated. The paucity of scientific research and lack of regulatory control over the industry places the burden of determining product quality, safety, and efficacy on the practitioner. Special consideration should be given to potential supplement-drug interactions in patients receiving traditional medical therapy.

The horse's medical record provides historic information on the animal's health status, health maintenance procedures, and medications. These factors should be evaluated to determine whether any of them are related to the horse's current nutritional state. This information is imperative to early nutritional intervention in the treatment of cases with established malnutrition, or to prevent malnutrition in at-risk animals.

FEED ASSESSMENT

To determine whether a given level of feed is adequate, feed quality should be determined by visual inspection. An important factor to assess when evaluating hay is the relative age of the forage at harvesting because younger plants contain more digestible energy and nutrients than older hay. Good-quality hay will be free of mold, dust, and weeds, and will have a high leaf-to-stem ratio with a green color that suggests that the hay was not excessively weathered. The energy, protein, vitamin, and mineral content of hay will vary with the geographic location of forage growth, the weather conditions during growth, and any alterations that have been made to the soil.

Because of the great variability in these factors, the only accurate way to determine the nutrient content of a feed is to analyze a representative sample. Core hay sampling devices should be purchased if large volumes of hay are analyzed frequently. Agricultural schools and local dairies may serve as a resource for occasional use of a core hay sampler. The practitioner should consult Lon Lewis' book *Equine Clinical Nutrition* for an explanation of proper sampling techniques. In cases where hay analysis is not performed, a rough estimation of the nutrient content of equine feeds can be obtained from the National Research Council (NRC) publication *Nutrient Requirement of Horses* (fifth revised edition, 1989).

PATIENT ASSESSMENT: BODY WEIGHT AND INITIAL EXAMINATION

Every horse that undergoes medical care or that is examined as part of a health maintenance program should have its body weight recorded on a routine basis. An accurate body weight measurement is essential to calculate the amount of feed needed and also enables the clinician to objectively assess the adequacy of the historical nutrition program of the patient. Subtle changes in body weight may be one of the only signs recognized in early disease states including hepatic and renal disease and internal abscesses. The most accurate measurement of a horse's weight is obtained through the use of a walk-on scale. Variability in gastrointestinal tract fill, the size of prior meals, and type of hay in the diet may result in significant variations (5%-10%) in body weight. This fact emphasizes the importance of a complete diet history for the patient, including meals fed on the day the horse is weighed. Dehydration can decrease the weight of the horse by as much as 5% to 8%. In an acutely ill equine patient, assessment of biochemical parameters including packed cell volume and plasma total protein concentration will enable the clinician to more accurately assess the severity of dehydration, and its effect on the horse's body weight. Serial weight measurements are a key component in the medical treatment of all equine patients.

Weight measurement with use of a walk-on scale is impractical in field situations, however, a fairly accurate estimate of a horse's body weight can be obtained with a weight tape. Weight tapes are often available from feed or tack stores and from feed manufacturers. An equine weight tape is used to measure the chest girth just caudal to the point of the elbow and is marked in pounds or kilograms of body weight that correspond to the girth measurement. A recent study confirmed that a weight tape gives a relatively good estimation of body weight in small ponies (< 350 kg, <14.2 hands) and large ponies (350-450 kg, as large as 14.2 hands), and a somewhat less accurate estimate of weight for Thoroughbreds and other horses of light build. The weight tape was least accurate in horses described as having a stockier build than the Thoroughbred, for which it resulted in an underestimation of body weight. Although the use of a weight tape may underestimate the actual weight of a horse, it is currently the best method of determining body mass in the absence of a scale. Estimation of a horse's weight by visual inspection is strongly discouraged. Studies show that even with years of experience most individuals cannot estimate a horse's weight with any degree of accuracy.

In addition to assessment of the equine patient's weight with a scale or a weight tape, the body condition score (BCS) of the animal should always be assessed to give an estimate of the long-term nutritional adequacy of the patient. The body condition scoring system gives a subjective evaluation of the patient's fat stores, and to a lesser extent, muscle mass. Changes in BCS are less affected by differences in body frame, and the BCS system gives a better assessment of body fat than the body weight measurement. Although good assessments of body composition are available for other species, this field remains in the experimental stage for equines. A description of the BCS system can be found in the NRC's *Nutrient Requirement of Horses* (fifth revised edition, 1989).

The system assigns a score of 1 to 9 on the basis of the amount of fat that is distributed over different regions of the horse's body. A score of 1 represents emaciation whereas a score of 9 is described as profound obesity. In the horse the most reliable site in which to assess a BCS is in the gluteal region with an evaluation of the ease of visibility of the tuber coxae, tuber ischii, and tailhead. Other sites that can be evaluated include the ribs, the shoulder and wither region, and the fat that covers the dorsal spinous processes; however, the amount of flesh that covers the ribs is poorly correlated with body condition score in horses. A body condition score of 1 to 3 indicates that the animal has a limited reserve of protein and fat to use for energy during periods of increased metabolic activity (local infection, generalized sepsis or recovery from surgery) or when the patient is hypophagic or anorexic. Horses with BCS of 3 or less require early intervention with nutritional therapy to improve the success of their recovery from an illness. Horses that have a BCS from 7 to 9 are obese and may suffer complications in lipid metabolism if their energy intake declines during periods of illness.

During the routine physical examination, a thorough oral examination should be performed. Dental abnormalities including missing teeth, malocclusions, retained deciduous teeth, abnormalities of wear, and premolar and molar hooks and points can all impair the ability of the horse to masticate, thus decreasing the digestibility of the diet. Evaluation of the stem length of digested fiber in the feces is a crude method to assess a horse's ability to properly masticate their forage, and although helpful it should not replace the oral examination. A proper oral examination includes flushing out the mouth with water before a visual examination. In a horse with chronic weight loss, a full mouth speculum examination is recommended to provide adequate visualization of the caudal molars and potential soft tissue damage from molar overgrowth. Proper alignment and restoration of the maxillary and mandibular arcades may take months to achieve. Although the procedures involved will not be discussed here, it is important to remember that abrupt changes in the dental arcades may lead to increased problems with mastication and persistent weight loss.

Concurrent with the therapeutic, surgical, and fluid plan of treatment for the acutely ill equine patient is the development of a feeding protocol. Horses that are evaluated for an acute illness often are anorexic. These patients will likely be dehydrated and may have electrolyte disturbances that can be partially managed with intravenous (IV) therapy, although complete repletion may require a return

to food consumption. Bloodwork, including a complete blood count and clinical chemistry panel, is routinely performed. Serum triglyceride levels should be performed on any patient at risk of either hyperlipidemia (triglyceride <500 mg/dl) or hyperlipemia (triglyceride >500 mg/dl). Ponies, donkeys, and obese horses (BCS, 7-9) appear to have an increased risk of hyperlipidemia and hepatic lipodosis during periods of anorexia. In a hospital setting, evaluation of both ionized calcium and ionized magnesium concentrations is recommended so that a fluid plan can be created to replete these minerals, if necessary. Protein bound calcium and magnesium are not biologically active, thus ionized samples should be analyzed. Although clinical and biochemical findings may identify abnormalities that can be managed by nutritional intervention, horses can become both protein and energy malnourished before any laboratory abnormalities are recognized. Early nutritional intervention in the acutely ill equine patient is an essential component of their successful recovery.

ENERGY AND PROTEIN REQUIREMENTS

The decision to institute nutritional support should be considered early in the treatment plan for the ill horse. Horses that are hypophagic or anorexic and consume less than their maintenance requirements for energy and protein for longer than 2 to 3 days should receive nutritional therapy. Delay in nutritional supplementation will increase the recovery time of the patient and will result in a loss of lean muscle mass that will delay the horse's return to athletic work. The disease may physically prevent adequate caloric intake (neurologic conditions that prevent food prehension or swallowing) or the horse may have a reduced appetite associated with the production of inflammatory mediators during periods of local or generalized sepsis. Horses may be able to eat but will have severe restrictions on the type and amount of food ingested, as is often the case for horses recovering from colic surgery. Institution of both calorie and protein supplementation for the postoperative colic patient, either through limited enteral nutrition or with partial or total parenteral nutrition (TPN) will limit use of endogenous protein and lipid stores for energy.

Current thinking among veterinary nutritionists is that every patient should consume at least enough calories to meet their daily resting energy requirements. In healthy horses confined to a metabolism stall, energy requirements are approximately 70% of the maintenance caloric needs for idle horses. This resting or *stall maintenance* energy requirement can be calculated from the following equation:

$$DE \text{ (Mcal/day)} = 0.975 + 0.021 (W)$$

where *DE* is the digestible energy, and *W* is the weight of the horse in kilograms. Similarly most sick or hospitalized horses are inactive and therefore do not have normal maintenance energy requirements. In human patients some disease states result in higher than normal maintenance energy needs (hypermetabolism). However, energy requirements for various disease states in horses are unknown and extrapolation from other species may have detrimental effects, because overfeeding can be as harmful as inadequate nutrition. Accordingly, the authors recommend that initial cal-

culation of energy requirements be based on the above equation. Importantly, it should be standard protocol to calculate a horse's energy requirements and record food intake on a daily basis to determine the adequacy of caloric intake and the need for nutritional support.

Initially the goal of nutritional support is to meet stall maintenance energy needs, followed by a gradual (during 3-4 days) increase in feeding until true maintenance energy requirements are achieved. Because horses are sensitive to acute changes in their diet, all changes in feed, either oral or parenteral, must be made gradually. Maintenance requirements (defined as the amount of DE required for zero body weight change plus normal activity of nonworking horses) of horses that weigh 600 kg or less can be estimated from the following equation:

$$DE \text{ (Mcal/day)} = 1.4 + 0.03 (W)$$

Equations for calculation of the DE requirements of horses that weigh more than 600 kg are provided in the NRC's *Nutrient Requirements of Horses* (fifth revised edition, 1989). It must be emphasized that these equations only provide an estimate of a horse's daily energy requirements. Even in healthy horses, actual energy needs may vary by as much as $\pm 25\%$. Ongoing measurement of body weight (excluding changes in weight caused by variations in hydration) will provide the best guide to the adequacy of energy intake and the need for adjustments. The amount of calories supplied should be adjusted as necessary.

Most often protein deficiency in a sick horse is the result of inadequate food intake. If a deficit exists in carbohydrate and fat intake, endogenous protein is used for energy and not for the horse's protein needs, resulting in an overall state of protein deficiency. Therefore it is fruitless to provide protein to meet protein requirements if energy needs are not being met. Crude protein (CP) requirements in the adult horse for maintenance may be estimated with the following equation:

$$CP \text{ (grams)} = 40 \times DE \text{ (Mcal/day)}$$

There is a paucity of information concerning the protein requirements for particular diseases in the horse, and therefore specific recommendations for each condition are only speculative. Unless contraindicated by the underlying disease (i.e., some renal and hepatic diseases), all horses should initially be fed to meet maintenance protein requirements.

WHEN TO INSTITUTE NUTRITIONAL SUPPORT

The type of nutritional therapy will depend on the nutritional condition of the horse, the duration of the disease, and the type of disease process. In general, any horse that fails to consume 75% of its stall maintenance and protein requirements for more than 48 hours is a candidate for nutritional support. However, earlier intervention is indicated in underconditioned and overconditioned horses. Patients with a low BCS (1-3) have smaller endogenous energy reserves and will benefit from early nutritional intervention. Even in preacute and acute disease states, supplementation of undernourished horses will improve their recovery and

prevent further depletion of both lean tissue and body fat mass. Similarly, early nutritional intervention is indicated in equids with high BCS (7-9), particularly ponies, donkeys, and Miniatures; even a short period of hypophagia or anorexia in these patients is associated with high risk for metabolic derangements in lipid metabolism that lead to hyperlipidemia, hyperlipemia, and hepatic lipidosis. Although these patients appear to have plenty of protein and energy reserves because of their overconditioned appearance, failure to treat these patients with nutritional support may result in secondary complications from hepatic lipidosis, which can be fatal.

Horses with body condition scores of 4 to 6 have more endogenous reserves that can supply both energy and protein during periods of hypophagia and anorexia. Nonetheless, despite the relatively greater reserves in these patients compared with undernourished horses, animals in this middle BCS range will also benefit from early nutritional intervention even during peracute and acute disease states. Calories and protein provided from either enteral or parenteral nutrition will enable these horses to preserve their lean body mass and fat mass, so a return to health and athletic performance will not be unduly prolonged. Traditionally, the anorexic or hypophagic horse has been offered a cafeteria-style diet or limited grazing in the hope that some feed will stimulate the horse's appetite enough for resumption of normal food intake. Although enticing the horse to eat with this method is useful, only a fraction of the necessary daily calories are usually consumed.

NUTRITIONAL INTERVENTION

To provide calories and protein to an equine patient that is not able or willing to eat, clinicians have two main routes for administration of the nutrients. The first, which for economic and technical reasons is usually limited to a hospital setting, is the administration of a parenteral diet. Total parenteral nutrition (TPN) is a safe, effective way of meeting calorie and protein needs through the provision of an IV solution of lipid, amino acids, glucose, and minerals (see Chapter 3.9: "Parenteral Nutrition for Colic Patients"). The second method of administration of caloric support is through the use of enteral diets. Enteral feeding is accomplished by the infusion of a liquid diet through a nasogastric tube. This method of dietary therapy is not appropriate for conditions in which the animal cannot tolerate esophageal tube or gastric feeding, or when there is a possibility that the horse will reflux and aspirate the infused contents (lateral recumbency, dementia, low head position, ileus). However, this method is the easiest and most cost-effective way to nutritionally manage a horse with hypophagia or anorexia, both in field and hospital settings. Esophagostomy tubes can be placed if the nasopharynx or proximal cervical esophagus of a patient is compromised. The reader is referred to the article by Freeman and Naylor in the supplemental readings list for a detailed description of procedures for placement and maintenance of esophagostomy tubes.

ENTERAL FEEDING

The field of enteral nutrition for equine patients continues to develop. Human enteral formulations (e.g., Vital HN or

Osmolite HN, Ross Laboratories, Columbus, Ohio) have been used with some success in horses. However, the cost of these formulations and the potential for horses to develop diarrhea during treatment frequently precludes the use of these products.

Because the horse appears to develop diarrhea if adequate fiber is not included in the diet, enteral formulations should provide a fiber source. An alfalfa/casein enteral formulation that supports body weight and maintains biochemical parameters within normal ranges in healthy adult horses is provided in Table 13.2-1. In addition to this enteral recipe, slurries can be made from complete pelleted feeds that have been soaked in water, and then blended to reduce the size of feed particles (Table 13.2-2). When a complete pelleted feed is used, the energy content of the pellets (which can be obtained from the manufacturer) should be compared with the energy requirements of the horse to determine the volume that must be administered in 24 hours to achieve 75% of the horse's energy needs ($DE \text{ [Mcal/day]} = 0.975 + 0.021 [W]$). It is important to gradually increase the volume of diet that is administered to prevent complications from delayed gastric emptying and colic that could develop subsequent to rapid feed changes.

Vegetable oils can be used to increase the caloric density of enteral diets because fat contains approximately twice the calories (on a weight basis) of protein or carbohydrate. The purpose of increasing the energy density of a diet is to increase energy intake or to decrease the amount of food necessary to meet an animal's energy requirements. Vegetable oils are highly calorie-dense and in a form amenable to tube feeding. As a result they can be very useful in patients receiving enteral supplementation, because delivery of sufficient calories in a limited volume can be critical to successful nutritional support. Vegetable oils can be added to a healthy horse's diet in amounts as high as 20% of solid feed, although 10% fat is a more realistic target in most situations ($\frac{1}{2}$ pint or 1 c per 5 lb of feed or 100 ml/kg feed). Note that 1 standard measuring cup holds 8 oz (250 ml) of water and approximately 200 g of vegetable oil, which provides 1.6 to 1.7 Mcal of DE (see Chapter 13.1: "Influence of Dietary Energy Sources on Health and Performance"). Vitamin E (100 IU per 100 ml oil) should be included when vegetable oil is added to the ration.

When providing supplemental fat to a sick horse (450-500 kg BW), $\frac{1}{4}$ to $\frac{1}{2}$ cup per day should be given initially and then gradually increased if no adverse response is seen (diarrhea, steatorrhea, or lipemia). Fat can delay gastric emptying and should not be supplemented in diets fed to horses with motility concerns until the clinician is certain of adequate gastrointestinal function. Supplemental fat should also not be fed in horses with hyperlipidemia. Not only does exogenous fat supplementation increase caloric density, but it also changes the nutrient balance of a diet. Care should be taken to ensure that fat supplementation does not lower protein or carbohydrate intake below the horse's requirements. This issue is of particular concern in protein-restricted diets.

Once the enteral formulation has been selected, it can be made into a puree with a blender to facilitate administration through a nasogastric tube. Pellets should always be soaked in water to soften the feed before it is put in the blender, and to prevent additional swelling of the feed

Table 13.2-1
Alfalfa/Casein Enteral Formulation and Recommended Tube Feeding Schedule for a 450-kg Horse*

Parameter	DAY						
	1	2	3	4	5	6	7
Electrolyte mixture (g)†	230	230	230	230	230	230	230
Water (L)	21	21	21	21	21	21	21
Dextrose (g)	300	400	500	600	800	800	900
Casein (g)‡	300	450	600	750	900	900	900
Dehydrated alfalfa meal (g)	2000	2000	2000	2000	2000	2000	2000
Digestible energy (Mcal)	7.4	8.4	9.4	10.4	11.8	11.8	12.2

Modified from Naylor JM, Freeman DE, Kronfeld DS: Alimentation of hypophagic horses. *Comp Cont Educ Pract Vet* 1984; 6(2):S93-S99.

*These allowances should be divided and administered into three or four feedings daily. Maintenance requirements for a 450-kg horse are 13 Mcal of digestible energy.

†Composition of electrolyte mixture: sodium chloride (NaCl) 10 g; sodium bicarbonate (NaHCO₃) 15 g; potassium chloride (KCl) 75 g; potassium phosphate (dibasic anhydrous, K₂HPO₄) 60 g; calcium chloride (CaCl₂·2H₂O) 45 g; magnesium oxide (MgO) 25 g.

‡Casein (Sigma-Aldrich, St. Louis).

Table 13.2-2
Complete Pelleted Feed Enteral Formulation and Recommended Tube Feeding Schedule for a 500-kg Horse*

Ingredient	Days 1 and 2 (½ Food)	Days 3 and 4 (½ Food)	Days 5 and 6 (½ Food)	Days 7 and 8 (Full Food)
Complete pelleted horse feed (g)†	1176	2352	3528	4858
Vegetable oil (ml)	118	236	354	472
Water (L)	8	16	24	24
Digestible energy (Mcal)	4	8	12	16.4

*Maintenance requirements for a 500-kg horse are 16.4 Mcal of digestible energy. These allowances should be divided and administered into a minimum of four feedings daily. At the discretion of the attending veterinarian, maintenance energy requirements may be reached in less than 8 days depending upon the horse's nutritional status and underlying disease.

†Equine Senior (Purina Mills, St. Louis), 1.2 Mcal/454 g.

particles once they have been administered into the stomach. The tube with the smallest possible internal diameter should be chosen for diet administration. Foal tubes with a ⅜-inch (8 mm) outer diameter are ideal, and can remain in place between periods of diet administration. However, large-bore tubes (internal diameter of 12.7 mm or larger) are often necessary for the efficient administration of slurry diets. Before placement of the nasogastric

tube, the administration equipment (pump, tube, and blended enteral diet) should be tested to ensure that the solution flows adequately. In some cases, the diet may need to be put in the blender a second time or further diluted by the addition of water. The end of the tube should be open-ended, rather than fenestrated, to prevent the tube from becoming clogged.

Ideally the enteral diet will be administered in 4 to 6 feedings in a 24-hour period. Approximately 6 to 8 L of the enteral solution can be administered to a 500-kg horse during each feeding; however, if the horse has been anorectic, the volume that can be tolerated may be less. To aid in the adaptation of the gastrointestinal tract to the enteral diet for a horse that has been anorectic, the infusion should be administered at a rate of ¼ total volume on day 1, ½ total volume on day 2, ¾ total volume on day 3, and the total volume on day 4. If administration of the enteral diet is performed within 1 to 2 days of anorexia or hypophagia, the amount administered can be increased during a 2-day period. Before the enteral diet is infused, the horse should be evaluated to ensure that there is no spontaneous reflux of feed from an earlier feeding. If feed is easily obtained from the nasogastric tube, then the feeding schedule will need to be adjusted with increased intervals between feedings. Frequent feedings that are small in volume are always recommended, however, field practitioners should not avoid enteral feeding in their patients if the diet can only be administered twice a day. Although equine patients treated with a twice-daily administration of an enteral diet may not receive enough calories to meet their maintenance requirements, the energy obtained from the enteral diet will decrease the endogenous protein and lipid use in these animals.

While the horse is being fed enterally, it is imperative that the volume of water that is infused and the volume that is consumed by the horse is monitored and recorded. Extra fluid in the enteral solution may be needed if the horse will not consume sufficient water to prevent dehydration.

Before placement of the nasogastric tube the exterior of the tube should be coated with a water-soluble lubricant. The tube should be positioned in the stomach before administration of the diet. Liquid consistency diets can be administered through a gravity flow system, however, most enteral diets will need to be administered with a stomach pump. After administration, the tube should be elevated to a position above the level of the nares so that it can be checked for spontaneous reflux, an indicator of excessive gastric distention. After the diet is infused, the tube should be flushed with water and then capped with a syringe case or syringe plunger to prevent reflux of the infused contents. If the tube is small in diameter, it can remain in place between feedings, with the tip of the tube located in the distal esophagus and the outer end taped to the horse's halter to prevent it from becoming dislodged. The horse should be housed in a small stall and monitored frequently to ensure that the tube is properly positioned. If the horse is being treated in the field, and the owner cannot monitor the animal between feedings, the tube should be removed and replaced for the next diet administration. Smaller tubes result in fewer esophageal complications and are recommended. If the tube becomes blocked, gentle water lavages can be used to dislodge the blockage.

Enteral diets are useful for both short-term and long-term nutritional support. The advantage of complete feeds for the enteral diet is that they provide the appropriate vitamins and minerals to meet the requirements of the horse. If prolonged enteral feeding is required or if the horse has increased losses of vitamins or minerals, then the diet may need to be supplemented to ensure that the appropriate nutrient balance is maintained. Horses appear to have similar electrolyte disturbances to other species when they are fed after a prolonged period of starvation. The refeeding syndrome is characterized by hypomagnesemia, hypophosphatemia, hypokalemia, glucose intolerance, and fluid intolerance. Clinicians who are faced with treatment of a horse that has been anorexic or starved for a prolonged period of time should closely monitor plasma electrolyte and glucose concentrations to avoid cardiovascular and neurologic complications, and to improve the recovery of their patients. Consultation with a nutritionist is recommended in the more complicated cases of nutritional management.

During treatment with enteral nutrition solutions, the horse must be monitored for signs of colic, gastrointestinal ileus, abdominal and gastric distention, and increased digital pulses. In addition to routine physical examination findings, ultrasound can be used to monitor gastric distention, and intestinal motility. Although anorexia will decrease the volume of feces produced, horses receiving enteral diets should still produce feces. Enteral diet supplementation should be discontinued if a horse develops diarrhea as a consequence of the treatment. Cases that are unresponsive to the enteral diet may require partial or total parenteral nutrition to support their energy and protein requirements.

Horses can be encouraged to eat even during the period of enteral diet treatment. If the nasogastric tube is too large

to permit uncomplicated swallowing of food, the tube should be removed between treatments. As is the case when initiating the enteral diet treatment, horses should be gradually weaned off from the enteral diet once they are able to consume 75% of their maintenance energy needs.

FIELD APPLICATION OF NUTRITIONAL SUPPORT

In nonhospital settings it is still feasible and recommended to integrate nutritional therapy into the management of sick horses. Assessment of body weight (with a weight tape) and BCS should be routine during physical examination. If weight loss is a part of the presenting complaint the owner should be questioned about the amount of food that is fed and the frequency of feedings. The quantity and quality of feeds provided should also be directly assessed. Although weight loss is a frequent presenting complaint, it is equally important to recognize the obese patient and to counsel the owner about proper management practices to reduce the weight of their horse. If nutritional inadequacy is determined to be the cause of weight loss, body weight estimates (weight tape measurements) can be used to calculate the daily caloric requirements. NRC guidelines for feed intake are helpful in estimating the amount of feed needed to meet the energy needs of the horse. If the horse is hypophagic or anorexic and nutritional support is required, and if no contraindications exist to administration of an enteral diet, then a nasogastric tube should be placed and an enteral diet administered following the guidelines discussed above. The diet can be prepared before the farm visit. Cases that are refractory to therapy may need more aggressive management with parenteral nutrition at a referral clinic.

Supplemental Readings

- Burkholder WJ, Thatcher CD: Enteral nutritional support of sick horses. In Robinson NE (ed): *Current Therapy in Equine Medicine*, 3rd edition, pp 724-731, Philadelphia, WB Saunders, 1992.
- Freeman DE, Naylor JM: Cervical esophagostomy to permit extraoral feeding of the horse. *J Am Vet Med Assoc* 1978; 172:314-320.
- Golenz MR, Knight DA, Yvorchuk-St Jean KE: Use of a human enteral feeding preparation for treatment of hyperlipemia and nutritional support during healing of an esophageal laceration in a miniature horse. *J Am Vet Med Assoc* 1992; 200:951-953.
- Lewis LD: Sick horse feeding and nutritional support. In Lewis LD (ed): *Equine Clinical Nutrition*, Baltimore, Williams & Wilkins, 1995.
- National Research Council: *Nutrient Requirements of Horses*, 5th revised edition, Washington, DC, National Academy Press, 1989.
- Reavell DG: Measuring and estimating the weight of horses with tapes, formulae and by visual assessment. *Equine Vet Educ* 1999; 1:188-193.
- Wiltham CL, Stull CL: Metabolic responses of chronically starved horses to refeeding with three isoenergetic diets. *J Am Vet Med Assoc* 1998; 212:691-696.

CHAPTER 13.3

Probiotics, Prebiotics, and Synbiotics

J. SCOTT WEESE

Guelph, Ontario, Canada

The equine gastrointestinal tract, particularly the large colon and cecum, contains a complex and diverse bacterial population that plays a critical role in maintenance of health. This microflora is essential for growth and survival of the animal and is critically important for the prevention of colonization or overgrowth of intestinal pathogens. The intestinal microflora can be protective via a number of mechanisms including competitive inhibition (occupation of specific environmental niches), production of inhibitory factors, modification of the local environment (production of organic acids, volatile fatty acids, hydrogen peroxide, and other compounds), or effects on local inflammatory and immune responses. Disruption of this microflora can result in the development of disease, which manifests most commonly as diarrhea. Antimicrobial therapy commonly is implicated; however, other factors such as stress, diet changes, transport, or concurrent disease may be involved.

Because of the critical nature of this microflora and the potentially disastrous results that can occur when it is disrupted, beneficially changing the microflora or preventing adverse changes is desirable. Modification of the intestinal microflora through the administration of prebiotics, probiotics, or synbiotics is becoming increasingly popular in human and veterinary medicine as a means to prevent or treat disease. One of the main factors limiting the use of probiotics in equine medicine is the paucity of objective research. Prebiotic therapy has received even less attention. A review of the current literature provides little to no guidance on how to incorporate successfully these treatment options into a therapeutic plan. Studies involving other mammalian species can be informative; however, interspecies variation limits direct cross-application of results.

PROBIOTICS

Probiotics are living microorganisms that when ingested in certain numbers exert a beneficial effect beyond that of their nutritional value. Probiotic therapy is not a new concept. Rather it dates back to at least 1905; however, interest in probiotic therapy has increased dramatically over the past 10 to 20 years. Probiotics are an attractive, nonantibiotic, safe, and potentially efficacious treatment option in horses and other species.

The exact mechanism of action of probiotics is still unclear. Initial theories revolved around “competitive exclu-

sion,” in which “good” bacteria eliminated or suppressed “bad” bacteria. Although competitive exclusion may play a role in probiotic therapy, it is unlikely to account for the wide array of beneficial effects that have been reported in other species. Alternative proposed mechanisms include antimicrobial factor production, immunoregulatory effects, antiinflammatory effects, anticarcinogenic effects, and direct effects on the intestinal mucosa (Box 13.3-1).

Most commercially available probiotics are non-spore-forming lactic acid bacteria, namely lactobacilli, bifidobacteria, and enterococci (Box 13.3-2). A variety of strains have been demonstrated to possess beneficial (probiotic) properties. Bacilli, including *Bacillus licheniformis*, *Bacillus subtilis*, and *Bacillus toyoi*, have been evaluated to a more limited extent, and are less widely available. One of the most attractive properties of bacilli is their ability to form resistant spores that should be better able to withstand the rigors of processing and storage. Nonpathogenic strains of *E. coli* have been evaluated in some species as a means of competitively excluding pathogenic strains of *E. coli*. Probiotics containing *E. coli* are not available for horses and may not be useful as the relevance of *E. coli* in equine gastrointestinal disease is unclear.

Yeasts also have been evaluated for probiotic properties; however, most yeast supplements act as nutritional supplements, not probiotics. *Saccharomyces boulardii* is a nonpathogenic yeast shown effective for the prevention of antibiotic-associated diarrhea and treatment of recurrent *Clostridium difficile* diarrhea in people. This effect is thought to be due to direct effects on *C. difficile*, in addition to secretion of a protease that affects toxins. Whether these same effects occur in horses and the dose required have not yet been reported. In people, a dose of 3×10^{10} CFU/d (30 billion viable organisms per day) has been used. Presumably, a higher dose would be required in adult horses. *Kluyveromyces fragilis* (*marxianus*) B0399 is a strain of yeast marketed for use in horses. It is claimed that this yeast can survive passage through the stomach and have various effects in the intestinal tract of the horse. This species of yeast may have increased heat stability and survival during processing and storage, which would be beneficial; however, *in vivo* studies are lacking.

Yogurt is used commonly in humans and animals for the treatment of enteric disease. Despite anecdotal reports of success, doubts have been raised about the efficacy of yogurt in people because of a number of reasons. Most yogurts contain *Streptococcus thermophilus* and *Lactobacillus*

BOX 13.3-1**Possible Mechanisms of Action of Probiotics****Competitive Inhibition**

Suppression of inflammation
Modification of the local environment
Consumption of potentially harmful products

Antimicrobial Factor Production

Immune regulation
Inactivation of procarcinogens

BOX 13.3-2**Examples of Commonly Used Prebiotics and Probiotics in People****Prebiotic**

Fructooligosaccharides (FOS)
Inulin
Galactooligosaccharides
Lactulose
Lactitol

Probiotic

Lactobacillus rhamnosus strain GG
Lactobacillus acidophilus
Lactobacillus casei
Lactobacillus reuteri
Lactobacillus plantarum
Enterococcus faecium
Bifidobacterium bifidum
Bifidobacterium longum
Bifidobacterium thermophilum
Saccharomyces boulardii

bulgaricus, which are not typically considered to be probiotics because of destruction during passage through the intestinal tract. Some commercial yogurt products contain specific probiotic strains and therefore may be useful, but the low bacterial numbers present in yogurt may limit their effectiveness. Commercial probiotic yogurts must contain 1×10^7 CFU/ml, but this level of growth is not present in all products. Without specific dose determination studies, predicting the volume of yogurt required for a probiotic effect in horses is difficult. However, with a yogurt product containing 1×10^7 CFU/ml, 30 liters per day would be required to deliver a dose of 3×10^{11} CFU/d. Although lower volumes of yogurt may be effective in some cases, using concentrated probiotic preparations containing higher levels of bacterial growth is preferable.

Although a number of organisms have been demonstrated to possess beneficial probiotic properties, great variation exists within species of microorganisms. Beneficial effects cannot be extrapolated between members of the same species, let alone the same genus. Individual bac-

terial or yeast strains must be tested to determine whether they possess beneficial properties. These include surviving passage through the stomach and small intestine, remaining viable during processing and storage, being non-pathogenic, and exerting one or more beneficial effects such as antimicrobial factor production, immune regulation, or decreasing inflammation. In the absence of strain-specific *in vitro* and *in vivo* testing, determination of whether a certain strain could be beneficial is impossible. Further, some believe that probiotic organisms should originate from the intestinal tract of their target species. Although this has not been evaluated in horses, it seems logical that microorganisms found in horses would likely be better adapted to survive in the intestinal tract of a horse compared with bacteria originating in other species.

Lactobacillus rhamnosus strain GG (LGG) is perhaps the best-tested human probiotic and has been demonstrated to be effective for the prevention or treatment of a number of conditions. However, high doses of this organism are required to achieve intestinal colonization in adult horses. Lower doses are able to colonize the intestinal tract of foals, however, so LGG may have potential for the prevention or treatment of diarrheic disease in foals.

In humans, certain probiotics have been demonstrated to be effective in a wide variety of conditions, including acute viral and nonviral diarrhea in children, inflammatory bowel disease, "traveler's diarrhea," and lactose intolerance. Mixed results have been obtained for the prevention of antibiotic-associated diarrhea and reduction of serum cholesterol levels. Preliminary research suggests that probiotics may be useful in the treatment of atopic dermatitis, food allergy, Crohn's disease, prevention of dental caries, and stimulation of the immune system. Probiotics also have been shown to reduce the levels of various fecal enzymes associated with metabolic activation of carcinogens and mutagens.

Commercial Probiotics and Feeds Containing Probiotics

A number of probiotic supplements are commercially available for use in horses, in the form of powders, pills, capsules, or pastes and generally include one or more species of *Lactobacillus* or *Enterococcus*. The numbers of viable organisms that products claim to contain varies greatly, with some containing very low and almost certainly subtherapeutic levels. Despite the widespread availability of commercial probiotics in horses, little objective research supports their use. In one study, the administration of a probiotics did not affect the shedding of salmonellae in horses hospitalized for colic or colic surgery. This does not discount the potential for probiotic therapy in horses, because no indication existed that the organisms used in this study possessed any *in vitro* or *in vivo* effects that could be useful.

One of the major problems in evaluating response to probiotics is the apparent deficiency in quality control among many commercial probiotics. A recent study of eight veterinary probiotics reported that the best product contained less than 2% of its label claim of viable numbers. Most products did not contain one or more of the listed contents and many contained organisms not listed

on the label. The results of this study were similar to studies evaluating probiotics intended for human use. This makes selection of commercial probiotics difficult. Some equine products claim to be probiotics but contain only "fermentation products." Fermentation products are by-products of bacterial growth and may contain enzymes synthesized by bacteria but not necessarily live organisms. These products claim that enzymes produced by the lactobacilli are beneficial; however, no evidence supports these claims. Regardless, these products cannot be considered probiotics if no viable organisms are present.

An increasing number of commercial horse feeds claim to contain probiotic organisms. Probiotic-containing feeds represent an easy way to administer probiotics for a prolonged period of time. However, whether the addition of probiotics to a feed is a realistic option is uncertain. The potential for loss of viability exists during processing, especially when heat or moisture are involved. Shelf-life also would be a concern with respect to maintaining viability. A study of dog and cat foods that claimed to contain probiotics reported that the number of viable organisms tended to be low and often a disparity existed between label claims and actual contents. Whether this was due to improper addition of the probiotic organisms or loss of viability during processing and storage is unclear. The apparently high level of supplementation that is required for an organism to colonize the intestinal tract of an adult horse may preclude the manufacture of probiotic-containing feeds. Probiotic-containing creep feeds or foal supplements may be a more reasonable option because a much lower number of organisms are needed for colonization of a foal's intestinal tract.

Safety

Probiotics are classified as "generally regarded as safe" (GRAS) and adverse effects are reported rarely. Concerns exist regarding the use of probiotics containing enterococci because these organisms are recognized opportunistic pathogens. Certain probiotic enterococci have been proved able to transfer the gene responsible for vancomycin resistance. For this reason, a movement is growing, particularly in Europe, to stop the use of enterococci as probiotics. The incidence of adverse effects from the use of enterococci in equine probiotics is presumably extremely low. However, because few concerns exist regarding the use of probiotic products containing lactobacilli and bifidobacteria, avoiding the use of enterococci as probiotics in horses may be reasonable. *Lactobacillus rhamnosus* strain GG, a human-origin probiotic, has been shown to affect intestinal antigen transport, perhaps through decreased uptake by large molecule transport pores. If this effect occurs in foals, the theoretical possibility exists that passive transfer of maternal antibodies could be affected. Until proven otherwise, avoiding the use of probiotics in foals less than 24 hours of age is wise.

Clinical Application

A number of possible indications exist for the use of probiotics in horses, which involve primarily gastrointestinal disease. Probiotics should be considered for the treatment

of acute and chronic diarrhea in adult horses and foals. When probiotics are coadministered with antibiotics (oral or parenteral), the probiotic organisms may be killed. Therefore knowing the antimicrobial resistance spectrum of probiotic organisms is important to determine whether coadministration with certain drugs is feasible. This is important especially with drugs such as metronidazole that are used commonly in the treatment of diarrhea.

Probiotics are an attractive option for the prevention of disease particularly during high-risk periods (i.e., antibiotic administration, concurrent disease, shipping) or during outbreaks of foal diarrhea. The role of the intestinal microflora in cases of colic is unclear; however, some cases of colic may occur as a result of changes in the intestinal microflora. However, the utility of probiotics for prevention of colic is questionable given the high dose of organism seemingly necessary for colonization of the intestinal tract of adult horses. Probiotic therapy may be best used prophylactically during times of high risk for the development of diarrheic disease. If probiotics are to be used for the prevention of disease during specific circumstances, therapy should begin approximately 3 days before the high-risk period. Long-term prophylactic therapy may be more reasonable in foals because of the lower levels of organism required for colonization.

Ideally, probiotic organisms with demonstrated ability to colonize the intestinal tract of horses and proven efficacy would be used. Until proven products become available, probiotic strains demonstrated to be effective in other species may be useful; however, differences apparently exist between species in the ability of certain probiotic strains to colonize and exert effects. Appropriate dosing is important and must be supported by *in vivo* testing in horses. In the absence of equine studies, very high levels of viable organisms presumably would be required to colonize the intestinal tract of the adult, whereas lower levels should adequately colonize foals. Avoidance of products containing enterococci may be wise because they can be opportunistic pathogens. In addition, probiotic strains of enterococci have been shown able to transfer antibiotic resistance (including vancomycin resistance) to pathogenic enterococci. At this point, administration of doses of 1×10^{10} CFU/d (10 billion viable organisms per day) in foals and at least 3×10^{11} CFU/d (300 billion viable organisms per day) in adult horses is recommended.

Although the quality control of many commercial products is doubtful, only products identifying their contents to the species level and stating a guaranteed level of live growth should be used. Product labels should be scrutinized carefully. If a product states only the level of growth present at manufacturing, not by the expiration date, then it should be avoided. Storage of commercial products can affect greatly product viability. Probiotics should not be exposed to fluctuations in temperature and should be kept cool.

PREBIOTICS

A prebiotic is a nondigestible food ingredient that beneficially affects the host by stimulating growth and/or activity of certain bacterial components of the intestinal microflora. Prebiotics are neither hydrolyzed nor absorbed in

the small intestine, are a selective substrate for potentially beneficial organisms in the colon, and alter the colonic microflora in a manner that produces beneficial effects. A number of food ingredients could act as prebiotics; however, the most commonly evaluated prebiotics are those that stimulate the lactic acid bacteria (lactobacilli, bifidobacteria, and enterococci) component of the microflora. These consist mainly of nondigestible fructooligosaccharides (FOS) and soybean oligosaccharides. After passing through the small intestine essentially unchanged, they are a nutritional substrate for certain types of colonic and cecal bacteria. FOS have been evaluated in other species and, in general, increase the concentration of colonic bifidobacteria. The ability of lactobacilli isolates to utilize FOS is variable. At this point, little is known about the role of bifidobacteria in horses, whereas it is known horses have a significant lactobacilli population.

Lactitol can stimulate the growth of certain lactobacilli; however, its effect in horses is unproven. Arabinogalactan supplementation was reported recently to decrease the incidence of diarrhea in foals in a preliminary study; however, the exact mechanism by which this was achieved is unclear and further research is required. Mannan-oligosaccharides are derived from the cell wall of the yeast *Saccharomyces cerevisiae* and have been used as a poultry-feed supplement to improve production parameters. The mechanism of action is purported to be adhesion and inhibition of pathogenic bacteria and improvement of immune function rather than direct effects on intestinal microbial population. Therefore they are not prebiotics. Mannan-oligosaccharides have been administered to horses; however, no efficacy studies have been performed.

Prebiotics may be administered as daily or intermittent supplements or incorporated into commercial diets. An advantage of prebiotic therapy over probiotic therapy is that viable microorganisms are not required. Viability of prebiotics should not be lost during standard processing and storage, as opposed to the situation with probiotics. The safety of prebiotics has not been evaluated in horses. Generally, prebiotics are assumed safe. However, alterations in the intestinal microflora could result in adverse effects, depending on what bacterial populations are stimulated. Colic and laminitis associated with lush, spring grass may be caused by ingestion of high levels of fructooligosaccharides (fructans) and subsequent effects on

the intestinal microflora. The possible risks of prebiotic administration, particularly in high doses, warrant further evaluation.

SYNBIOTICS

Synbiotic describes a combination of a prebiotic and a probiotic. The addition of an appropriate prebiotic may improve survival and establishment of a probiotic organism by providing a readily available nutritional source that might not be used by competing organisms. However, this approach cannot yet be recommended in horses pending the identification of prebiotics and probiotics with demonstrable efficacy in the horse and compatible prebiotic/probiotic combinations.

CONCLUSION

The therapeutic use of prebiotics, probiotics, and synbiotics in veterinary medicine is in its infancy. Despite the widespread availability of these products little equine-specific research is underway. As a result, making educated decisions regarding the incorporation of these products into a treatment regimen is difficult. Given proper research, probiotics likely will become a useful and practical therapeutic option for the equine veterinarian. Prebiotics and synbiotics may be similarly useful; however, their potential is less clear. Given the apparent high index of safety of most commercially available probiotics, they may be used as an adjunctive treatment of gastrointestinal disease.

Supplemental Readings

- Collins MD, Gibson GR: Probiotics, prebiotics, and synbiotics: approaches for modulating the microbial ecology of the gut. *Am J Clin Nutr* 1999; 69:1052S-1057S.
- Parraga ME, Spier SJ, Thurmond M et al: A clinical trial of probiotic administration for prevention of *Salmonella* shedding in the postoperative period in horses with colic. *J Vet Intern Med* 1997; 11:36-41.
- Weese JS: Microbiologic evaluation of commercial probiotics. *J Am Vet Med Assoc* 2002; 220:794-797.

CHAPTER 13.4

Nutritional Support in Selected Metabolic, Hepatic, Urinary, and Musculoskeletal Conditions

MERI STRATTON-PHELPS

ANDREA J. FASCETTI

Davis, California

RAYMOND J. GEOR

Guelph, Ontario, Canada

This chapter discusses dietary recommendations for horses with selected acute and chronic disorders. It should be recognized that, for the most part, scientific evaluation of these dietary interventions is lacking. Nonetheless, clinical experience indicates that the nutritional support protocols described here can be beneficial when used with other treatment measures.

METABOLIC AND ENDOCRINE CONDITIONS

Obesity

Although the prevalence of obesity in equids is poorly defined, anecdotal evidence suggests that many horses and ponies are overweight. Ponies, Miniature Horses, and broodmares appear to be especially prone to excessive weight gain. The criteria for a diagnosis of obesity in horses and ponies have not been established. However, subjectively a horse or pony is considered overweight at a body condition score (BCS) of 7 (with a scale of 1 to 9), fat at a BCS of 8, and obese when the condition score is 9. In mature horses of body mass 480 to 580 kg, an increase in condition score of 2 units (from 4 to 6) is associated with weight gain of 33 to 45 kg (73-100 lb). This fact implies that each unit of condition score is approximately 17 to 22 kg (37-48 lb) in horses of this weight range. For most horses, a BCS of 5 is considered ideal. Therefore a mature lightbreed horse (e.g., Thoroughbred, Quarter Horse) with a BCS of 8 or 9 may be overweight by 70 to 80 kg.

The most common cause of obesity in horses and ponies is overfeeding in relation to energy requirements. Many owners overestimate the energy needs of their horse(s), particularly those that spend much of the day confined in stalls or small holding pens. The maintenance feeding recommendations furnished by feed manufacturers and the National Research Council (NRC) are best applied to horses maintained at pasture; for horses kept in confinement for much of the day, these feeding levels may exceed daily energy needs by 20% to 30%. Furthermore the energy expenditure (and therefore energy require-

ments) associated with light riding activities also tend to be overestimated. The energy requirement (above the maintenance need) associated with 1 hour of combined walk/trot exercise is approximately 2 to 3 kcal of digestible energy (DE) per kg bodyweight (i.e., 1.0-1.5 Mcal for a 500-kg horse). Realistically the energy needs of horses ridden in this manner once or twice per week should be based on maintenance requirements rather than the requirements for "working" horses. Some owners also have a poor understanding of the energy content of different feedstuffs. Forage (hay) is often regarded as "filler" that delivers few calories to the horse. The practice of feeding by the unit measure (e.g., a coffee can full of grain or section of hay) rather than by weight also contributes to overfeeding.

Obesity also may be a pathophysiologic manifestation. Hypothyroidism is frequently implicated as a cause of weight gain and obesity in horses. However, although the serum concentrations of the thyroid hormones are sometimes low in overweight horses, thyroid function in response to injection of thyroid-releasing hormone (TRH) is usually normal, thus precluding a diagnosis of hypothyroidism. More recently, a syndrome of obesity and recurrent laminitis associated with increased cortisol synthesis in peripheral tissues has been described (see following discussion and Chapter 16.3: "Peripheral Cushingoid Syndrome ['Equine Metabolic Syndrome']").

Management of uncomplicated obesity associated with overfeeding involves a reduction in caloric intake and an increase in physical activity. As a general recommendation, the diet should provide no more than 65% to 70% of maintenance energy requirements at the horse's ideal or target weight. However, it is imperative that the clinician determine the horse's current caloric intake and use these data in formulating recommendations for weight management. Some horses appear to gain weight when daily caloric intake is at or even below appropriate maintenance allowances. Drastic reductions in energy intake (a greater than 50% decrease in daily DE intake) are not advised, particularly in obese ponies, donkeys, and Miniature Horses because of the risk of hyperlipemia. As an example,

assume that an obese horse (BCS, 9) weighs 600 kg but its ideal weight is approximately 500 kg. The maintenance DE requirement for a 500-kg horse is 16.4 Mcal/day (Box 13.4-1). Therefore, the maximum daily intake should be $0.7 \times 16.4 = 11.5$ Mcal DE per day. Nonlegume hays such as timothy, brome, oat, Coastal, or Bermuda hay are preferred. Although the energy density of these hays varies, an average value is 0.8 Mcal DE per lb. Therefore, as a starting point the horse should be fed $11.5 \text{ Mcal} \div 0.8 \text{ Mcal/lb hay} = 14$ lb of hay. The hay allotment should be weighed with a portable or hand-held scale and divided into at least two feedings per day. The horse must be kept in a dry lot or box stall bedded with shavings or a similar unpalatable material. No grain or protein supplement should be fed, but provision of a vitamin-mineral supplement and/or trace mineral block is recommended. Water and salt should be available free choice.

An increase in daily energy expenditure is also essential for weight reduction. For previously sedentary horses, the increase in physical activity should be gradual, starting with 10 minutes of trot on a lunge line and building to longer sessions in a round pen interspersed with riding activity. Obviously an increase in physical activity is not possible in horses with musculoskeletal disease. Regular assessments of bodyweight (heart girth measurement) and BCS should be made. The rapidity of weight loss will vary greatly between horses. In a recent study, horses that initially weighed 522 to 634 kg (BCS, 5-6) had lost approximately 45 kg after 70 days of consumption of a diet that provided 70% of energy requirements for moderate exercise. These horses were also subject to physical conditioning 5 days per week. In most cases, a 3 to 5 month time-frame is realistic for achievement of ideal bodyweight. The

feeding program should be reassessed once the goal weight is reached.

Hyperlipemia

Hyperlipemia is characterized by hypertriglyceridemia and fatty infiltration of body organs, particularly the liver and kidneys. This condition primarily occurs in ponies, donkeys, and Miniature Horses, and is rarely diagnosed in horses. The incidence of hyperlipemia is higher in mares than in stallions and geldings, independent of reproductive status. The underlying pathophysiology of hyperlipemia involves negative energy balance, rapid mobilization of nonesterified fatty acids from adipose tissue, and increased synthesis and secretion of very-low-density lipoprotein (VLDL) triglycerides by the liver. However, the liver's capacity for VLDL synthesis is overwhelmed such that triglycerides accumulate in the liver and, eventually, other organs. Negative energy balance may result from poor nutrition, complete or partial anorexia associated with disease or other recent stress, the increased demands of pregnancy or lactation, or enforced feed restriction in the management of laminitis or oral or esophageal disease. Relative insulin resistance associated with obesity contributes to exaggerated and uncontrolled lipolysis under negative energy balance. The clinical signs of hyperlipemia include icterus, weakness, ataxia, severe depression, and dependent edema. In severe cases signs of hepatic failure may predominate. The presence of increased plasma triglyceride concentrations (>500 mg/dl) confirms the diagnosis. The clinician must be alerted to the possibility of hyperlipemia in any pony or donkey with the aforementioned risk factors (e.g., illness, anorexia, pregnancy, lactation, obesity). Although the reported mortality associated with hyperlipemia is very high (60%-80%), a successful outcome is possible with early diagnosis and initiation of therapy, including treatment of the underlying disease, correction of dehydration, electrolyte and acid-base disturbances, and nutritional support.

The primary objective of nutritional intervention is improvement in energy intake and balance. Animals free from an oral or intestinal disease that precludes feed intake should be offered a variety of palatable feeds (e.g., fresh green grass, leafy alfalfa hay, bran mash or grain mixed with molasses) to encourage intake. However, given the very rapid progression of the disease and the fact that most affected animals have a poor appetite, enteral or parenteral feeding (or a combination of the two) is recommended for achievement of positive energy balance. Suitable diets for enteral feeding include commercial "complete feeds" (feeds that deliver complete nutrition including forage/fiber) or a hand-mixed formula that includes alfalfa meal, dextrose, casein, and a vitamin/electrolyte mix (see Chapter 13.2: "Clinical Assessment of Nutritional Status and Enteral Feeding in the Acutely Ill Horse"). Digestible energy (DE) requirements should initially be calculated from the formula developed for stall rested horses (see Box 13.4-1). However, for long-term nutritional support (more than 3-4 days), use of the maintenance DE requirement (see Box 13.4-1) is advisable (~ 33 kcal/kg/day for horses weighing 400 to 600 kg; note that this value increases to 37 kcal/kg for a 200-kg horse, and to 44 kcal/kg for a 100-kg horse). A

BOX 13.4-1

Equations for Digestible Energy and Crude Protein Requirements in the Adult Horse

Estimation of daily DE requirements (Mcal/day) for horses confined to a stall:

125- to 856-kg body weight

$$DE = 0.975 + 0.021 (W)$$

Estimation of daily DE requirements (Mcal/day) at maintenance:

200- to 600-kg body weight

$$DE = 1.4 + 0.03 (W)$$

More than 600-kg body weight:

$$DE = 1.82 + 0.0383 (W) - 0.000015 (W)^2$$

Estimation of CP requirements (g/day):

Horses at maintenance levels

$$CP = (40) (\text{Mcal of DE/day})$$

Modified from National Research Council (NRC): Nutrient Requirements of Horses, 5th revised edition, Washington, DC, National Academy Press, 1989.

W, Weight of the horse in kilograms; DE, digestible energy; CP, crude protein.

recommended maximum total daily feeding volume is 35 ml/kg BW (e.g., 3.5 liters for a 100-kg animal). With an enteral diet nutrient density of approximately 1 kcal/ml, this feeding volume should allow delivery of maintenance DE needs. The total daily ration should be divided into frequent small feedings (6-12 per day). Initially one third to one half of the daily energy allowance should be fed with the full allowance given by day 3 or 4. Similarly as voluntary feed intake increases, a gradual withdrawal of enteral feeding is recommended to avoid relapse.

To prevent exacerbation of hypertriglyceridemia, the enteral diet should not contain added fat (e.g., corn or soy oil). Although human enteral formulas (e.g., Osmolite HN or Vital HN, Ross Laboratories, Columbus, Ohio) that provide as much as 30% of calories from fat have been used in the successful management of hyperlipemia, this level of fat may be excessive for many equine patients. The use of human enteral diets in horses has been associated with development of diarrhea, perhaps as a result of low dietary fiber intake. The risk of diarrhea may be reduced by feeding dehydrated alfalfa meal (as much as 300-350 g/100 kg/bwt/day), in addition to the commercial enteral diet. Further details on the use of enteral diets and diet formulations can be found in Chapters 13.2 and 13.4.

Complete parenteral nutrition (PN) may be required for patients with compromised gastrointestinal (GI) function such as horses affected by ileus and gastroesophageal reflux. The administration of a 5% dextrose solution is the simplest form of parenteral nutritional support and is recommended for the first 1- to 2-day period of treatment (at a rate of 2 ml/kg/hr), even in patients receiving enteral nutritional support. However, a 5% dextrose solution cannot provide adequate calories and should not be used as the only nutrient source. Therefore PN solutions that include amino acids, dextrose, vitamins, lipid, minerals, and electrolytes are recommended for patients needing longer-term parenteral support (see Chapter 13.5: "Nutritional Therapy in Gastrointestinal Disease" and Chapter 3.9: "Parenteral Nutrition for Colic Patients"). Parenteral feeding in obese, hyperlipemic patients is frequently complicated by glucose intolerance secondary to insulin resistance. Furthermore use of lipid-containing PN solutions can exacerbate hypertriglyceridemia. Therefore frequent monitoring of plasma glucose and lipid concentrations and, if necessary, adjustment of the PN composition and rate of administration are recommended. Insulin (protamine zinc insulin, 0.1-0.3 IU/kg IM q12h) can be administered to improve glucose tolerance, and heparin (100-200 IU/kg q12h) may help with lipid tolerance by enhancing the clearance of triglycerides from plasma.

Hyperadrenocorticism

Functional hyperplasia of the pituitary pars intermedia is the most common cause of hyperadrenocorticism in horses and ponies (Chapter 16.2: "Pituitary pars intermedia dysfunction—Equine Cushing's Syndrome"). Central to the pathophysiology of equine Cushing's disease (ECD) is a loss of feedback regulation of adrenocorticotrophic hormone secretion, with resultant adrenal cortical hypertrophy and hypercortisolemia. No cure exists for this condition, but drugs to suppress hormone secretion from the

pars intermedia (e.g., pergolide) can result in marked clinical improvement and a return to function. Although no published information is available on nutritional therapy in the management of ECD, the high incidence of hyperglycemia and relative insulin resistance (type 2 diabetes mellitus), recurrent laminitis, and poor body condition (muscle wasting) often dictates special feeding recommendations.

More recently, a "peripheral cushingoid syndrome" has been described in horses with obesity-associated laminitis (see Chapter 16.3: "Peripheral Cushingoid Syndrome ['Equine Metabolic Syndrome']"). This condition is thought to be caused by hypercortisolemia secondary to increased activity of the enzyme 11- β -hydroxysteroid dehydrogenase in adipose tissue. Similar to classic ECD, insulin resistance and glucose intolerance have been observed in horses with obesity-associated laminitis.

The diet of affected horses and ponies with evidence of insulin resistance and glucose intolerance (e.g., persistent hyperglycemia) should be low in soluble carbohydrates (i.e., starch and sugar). Good-quality forage such as timothy or oat hay should be the predominant dietary component. A protein, vitamin, and mineral supplement (1-2 lb/day of a 30% protein product for a 450-kg horse) is also recommended. If a higher daily caloric intake is required to effect weight gain, a highly fermentable fiber source such as sugar beet pulp (2.35 Mcal DE per kg) is recommended. Additional calories also may be provided in a vegetable fat such as soy or corn oil. However, because dietary fat is associated with the development of insulin resistance in other species, high-level dietary fat supplementation (>5% of the total diet) is not recommended. In older horses and ponies (>15 years), particularly those with dental abnormalities, a commercial "senior" feed is suggested. These feeds provide complete nutrition, including the fiber component of the diet, and are both highly digestible and low in starch and sugar (<20% by weight).

Some clinicians have recommended the oral administration of chromium and magnesium to horses with ECD (and recurrent laminitis) as a means to enhance insulin sensitivity. In other species, and to a more limited extent in horses, evidence exists that an increase in dietary chromium is associated with improved glucose tolerance. The mechanism of this effect is not known. The rationale for magnesium supplementation is less clear, although limited data from humans have demonstrated that low plasma total magnesium concentrations are associated with relative insulin resistance. The effect of chromium and magnesium supplementation on insulin sensitivity and glucose tolerance in horses with ECD has not been evaluated, and further research is required.

Horses and ponies with ECD are prone to opportunistic microbial infections. Accordingly the diet should provide adequate selenium (0.3 ppm or 3 mg/kg of diet), zinc (200-220 ppm), and vitamin E (at the minimum 200 IU/kg diet, with supplemental provision of 1000-2000 IU/day), nutrients thought to be important for nonspecific immunity.

Hepatic Disease

See also Chapter 3.26: "Liver Disease." Feeding recommendations for horses with hepatic dysfunction will vary

according to the severity of disease. Patients with hepatic encephalopathy (HE) are usually anorectic and some form of enteral or parenteral nutrition (or a combination) is necessary until appetite returns. Because blood glucose concentrations are often decreased in horses with fulminant hepatic failure, a continuous intravenous infusion of 5% dextrose (2 ml/kg/hr) can be beneficial during the transition to enteral nutritional support. Most equine texts recommend a low protein diet with a high ratio of branched-chain amino acids (BCAA) to aromatic amino acids (AAA) for horses with HE. The rationale for this recommendation is the hypothesis that high plasma concentrations of AAA (tryptophan, phenylalanine, tyrosine) favor an increase in the synthesis of encephalogenic "false neurotransmitters" in the brain. Because the clearance of plasma AAA is dependent on hepatic metabolism, the concentrations of these neurotransmitters can increase with hepatic insufficiency. Moreover, deficits in energy intake by hypophagic or anorectic animals increase the use of BCAA (leucine, isoleucine, and valine) as energy substrates and exacerbate the decrease in the BCAA:AAA ratio. Together these mechanisms contribute to increased transfer of the AAA across the blood-brain barrier.

However, the results of clinical trials in other species, including humans, are equivocal with respect to the benefit of diets high in BCAA in patients with HE. Given that the accumulation of ammonia plays a central role in development of HE, a more important consideration is provision of sufficient dietary energy (glucose precursors) and protein to ameliorate the breakdown of endogenous protein and subsequent ammonia buildup.

Provision of a balanced diet that provides adequate energy and protein (see Box 13.4-1) is the most important consideration when a plan is developed for nutritional support of the patient with hepatic failure. The diet should contain sources of readily available soluble carbohydrates such as molasses, maltodextrins, or starch. Frequent feedings (e.g., every 4-6 hours) may help to stabilize blood glucose concentrations and limit enteric ammonia production. The oral administration of lactulose (0.3 ml/kg every 6 hours) has been recommended as a means to limit absorption of enteric ammonia in horses with HE. However, this treatment is very expensive and frequently results in development of diarrhea. For these reasons, many clinicians now favor the use of oral neomycin and/or metronidazole as a means to suppress enteric ammonia production.

When appetite returns and during convalescence from hepatic failure, continued provision of a low-protein (~10% crude protein), highly digestible diet is recommended. Restriction of dietary protein intake is not necessary unless the horse demonstrates signs of hepatic encephalopathy. Oat or grass hay is the preferred forage; alfalfa and soybean meal should be avoided because of their high protein content. Additional calories can be provided in the form of beet pulp, cracked or flaked corn, and/or vegetable oil. Both corn and beet pulp are good sources of BCAA. Fortification with a supplement that contains water and fat-soluble vitamins is also recommended. Any supplements that are fed should be evaluated to ensure that hepatotoxic compounds are not included in the ingredients.

URINARY TRACT DISEASE

Renal Failure

The uremia, acid-base, and electrolyte disturbances that are associated with renal failure (see Chapters 17.8: "Acute Renal Failure" and 17.9: "Chronic Renal Failure") can decrease a horse's appetite and result in the need for nutritional support. In these patients, sufficient calories should be administered to meet at least 75% of maintenance DE requirements (with the stall confinement equation provided in Box 13.4-1) either through enteral feeding or parenteral nutrition. Once the horse is able to consume a maintenance amount of calories and protein, and is metabolically stable, the diet can be evaluated and altered to facilitate longer-term management of the renal disease. Changes to the diet should not be made abruptly during the acute period if the horse is anorectic or hypophagic. Rapid feed changes can result in GI complications and may preclude the return of the patient's appetite if the feed is unfamiliar and less palatable than the previous diet.

Studies in humans and small animal species with renal failure have demonstrated a beneficial effect of protein restriction. Because protein is a good source of phosphate, protein restriction results in phosphorus restriction. Uremic toxins (urea, creatinine, guanidine and its derivatives, and ammonia) produced from protein catabolism and phosphorus are detrimental to kidney health in patients with established renal failure. Protein intake in the equine patient with renal failure must be balanced to avoid both excess dietary protein that can lead to complications from azotemia and protein malnutrition that can lead to increased morbidity and mortality. The nutritional goal for horses with renal failure is to provide a diet with a maintenance level of good quality, highly digestible protein. A 500-kg horse at maintenance requires 16.4 Mcal DE per day and 656 g protein/day (see Box 13.4-1).

Young forages and legume hay contain a relatively high percentage of protein, and are generally not recommended for horses with renal failure. High-quality grass hay is generally the best forage for horses with renal failure, however, some grass hay contains such a low concentration of protein, that if fed without consideration of the protein content, the horse may develop protein malnutrition. Ideally the horse should be fed a diet with 10% to 11% protein, provided the protein requirements of the animal are met to avoid the development of protein malnutrition. Feed analysis is the most direct method of determining the true protein and phosphorus content of the feed, and is always recommended, although rough estimates can be obtained from the NRC nutrient tables. Ration balancing and the creation of a therapeutic diet for the equine patient will ensure that the proper concentrations of nutrients are fed. If additional energy or protein is required, the diet of the horse can be supplemented with grain, commercial grain mixes, commercially produced complete feeds, pelleted feeds, or protein supplements, and/or a source of vegetable fat such as corn oil. Corn or soy oil provides a source of concentrated calories, with 1.9 Mcal per cup (1.6-1.7 g). Because addition of fat to the diet may increase the production of oxygen free radicals because of peroxidative damage, supplemental vitamin E (at the minimum, 100 IU per 100 ml of oil) should be added

to the diet. Vitamin E added to the diet in capsule form is palatable and is consumed by most horses. Salt (NaCl) should be available free choice.

Dietary phosphorus restriction in dogs with experimentally induced chronic renal failure resulted in a marked increase in survival time compared with dogs without phosphorus restriction. The effects of phosphorus restriction in horses with renal failure has not been experimentally determined, however, the benefits to renal health are expected to be similar to other species, and a reduction in the level of phosphorus in the diet is recommended. The diet of horses with renal failure should not exceed the NRC's 1989 recommendation of 0.87 g phosphorus per Mcal DE per day. Bran products (e.g., wheat bran and rice bran) should be avoided because of their high phosphorus content.

Renal disease is a dynamic process, and clinical and biochemical parameters must be monitored throughout the course of the disease. Alterations in the levels of dietary protein and phosphorus may be necessary if the horse develops biochemical or clinical signs of protein malnutrition, hyperphosphatemia, or uremia. If the patient develops hypercalcemia the diet should be mildly restricted in calcium, however, calcium should be fed at a maintenance level (1.22 g calcium/Mcal DE/day) for other renal failure patients.

Urinary Tract Calculi

The dietary management of equine patients with calcium carbonate urinary tract stones is focused on the prevention of additional crystal formation. Although most calculi form in the bladder, some horses will develop nephroliths and ureteroliths instead of or in conjunction with uroliths. The following recommendations are designed to aid in the prevention of recurrent urolithiasis, however, in some horses new stones may form despite dietary management. Surgical intervention is recommended in all horses with urinary tract calculi because dietary management is not thought to dissolve the stones.

Strategies to increase water intake are the cornerstone of dietary management for urinary tract calculi. Diuresis should decrease crystal aggregation and stone growth. Addition of salt to the diet may induce a relative diuresis as a result of increased water consumption. Sodium chloride does not appear to increase the renal excretion of calcium in the horse, as in other species, and can be added to the diet (90 g/day) to increase water consumption. The dose should be titrated to achieve a urine specific gravity of less than 1.020 in patients with urinary tract stones.

Calcium carbonate calculi form in an alkaline pH. Dietary therapy to lower the urinary pH (≤ 7) includes feeding an anionic ration, or treatment of the horse with urinary acidifiers (ammonium chloride (50-200 g/day), ammonium sulfate (35 g/day), oral D-L methionine (500 grams per day), or L-ascorbic acid (500 g/day). It should be remembered that dietary acidification results in an increase in renal calcium excretion, so acidification therapy should be conservative. Regardless of the method chosen to change the horse's urine pH the owner should monitor urine pH once or twice weekly, and routine urinalyses should be performed to monitor urine specific gravity. Al-

though ammonium chloride is frequently used in the management of equine urolithiasis, the long-term safety and efficacy of urinary acidifiers has not been evaluated in the horse. The diuresis that results from treatment with ammonium chloride or ammonium sulfate may explain the apparent efficacy of these acidifiers in reducing stone recurrence. Treatment with urinary acidifiers is often problematic because of the low palatability of the treatments, thus manual administration of the acidifying agent is required. Oversupplementation with the acidifiers may result in subclinical or clinical metabolic acidosis that can adversely affect the animal and result in a decrease in the urinary concentration of citrate, an important crystal-inhibiting substance. Because of the limitations associated with the administration of urinary acidifiers, a reduction of the urine pH with a low dietary cation-anion balance diet (DCAB) is recommended.

The feeding of a low-DCAB diet can result in decreased urine pH and may inhibit calcium carbonate urolith recurrence. Use of DCAB formulas to balance a ration requires that the levels of anions (Cl^- , S^{2-} , P^{3-}) and cations (Na^+ , K^+ , Ca^{2+} , Mg^{2+}) be measured in both the forage and grain components of the diet. The most accurate measurements of ion content are obtained from feed analysis of core hay samples or grain products. The mineral contents of forage and single component grains can be roughly estimated from the feed tables listed in the NRC publication *Nutrient Requirements of Horses* (fifth revised edition, 1989). However, to obtain chloride concentrations other NRC publications must be referenced. Although the guaranteed analysis of feed components listed on a commercial bag of feed can be used as a guideline, feed analysis is recommended because concentrations of the required ions are not always provided. The ionic content of any supplements must also be evaluated.

To create a low DCAB diet, the horse can be fed one type of forage, a combination of forages, or forages and concentrates. The target DCAB should be between 200 to 300 mEq/100 g diet dry matter (DM). Once the horse has been adapted to the diet, urine pH should be checked by the owner once or twice weekly to ensure that pH is 7 or less. The equation used for DCAB calculation and one sample calculation are shown in Box 13.4-2. Legume hays tend to have an increased content of potassium that results in a higher DCAB, whereas oat and grass hays and grain tend to have a lower DCAB. Legume hays should be avoided in the ration of horses with calcium carbonate calculi to achieve a lower DCAB, and to avoid excess dietary calcium.

The level of calcium in the diet of horses that have formed calcium carbonate calculi should meet NRC requirements of 1.22 g calcium/Mcal DE/day. Excess dietary calcium may result in greater intestinal calcium absorption (provided that the calcium is not complexed to substances in the GI tract such as oxalate and phytate), and a greater excretion of calcium in the urine. Diets that are deficient in calcium will result in elevated PTH, and an increase in calcium transport from the small intestine to the blood. Excess dietary phosphorus also decreases calcium absorption in the small intestine. Although disorders of calcium metabolism have been associated with the formation of calcium-containing urinary tract stones in other

BOX 13.4-2

Equations to Calculate the Dietary Cation-Anion Balance of Equine Rations

DCAB equation

$$[(\text{mEq Na}^+ + \text{mEq K}^+ + 0.15(\text{mEq Ca}^{+2}) + 0.15(\text{mEq Mg}^{+2})) - [\text{mEq Cl}^- + 0.25(\text{mEq S}^{-2}) + 0.5(\text{mEq P}^{-3})]]$$

To change As Fed (AF) concentrations to DM:

$$\frac{\% \text{ AF}}{\% \text{ DM}}$$

(For example, if Ca^{+2} is 1.24% AF, and the feed is 90% DM, then $1.24/0.90 = 1.37\%$ DM.)

To change concentrations in % DM to mEq:

$$\% \text{ DM} \times \text{Conversion factor} = \text{mEq}$$

Element	Conversion Factor
Na^+	435
K^+	256
Ca^{+2}	499
Mg^{+2}	823
Cl^-	282
S^{-2}	624
P^{-3}	581

Revised DCAB equation with mEq calculations

$$[(\% \text{Na}^+ \times 435) + (\% \text{K}^+ \times 256) + 0.15(\% \text{Ca}^{+2} \times 499) + 0.15(\% \text{Mg}^{+2} \times 823)] - [(\% \text{Cl}^- \times 282) + 0.25(\% \text{S}^{-2} \times 624) + 0.5(\% \text{P}^{-3} \times 581)] \text{ mEq per 100 g DM}$$

Sample Calculation, Oat Hay*

1. Identify cations and anions in %DM:

Cations: $\text{Na}^+ = 0.41\%$, $\text{K}^+ = 0.61\%$, $\text{Ca}^{+2} = 0.23\%$,
 $\text{Mg}^{+2} = 0.17\%$

Anions: $\text{Cl}^- = 0.36\%$, $\text{S}^{-2} = 0.18\%$, $\text{P}^{-3} = 0.15\%$

2. Set up DCAB equation:

$$[(0.41 \times 435) + (0.61 \times 256) + 0.15(0.23 \times 499) + 0.15(0.17 \times 823)] - [(0.36 \times 282) + 0.25(0.18 \times 624) + 0.5(0.15 \times 581)] \text{ mEq/100 g DM}$$

$$\text{DCAB} = 198 \text{ mEq/100 g DM}$$

Sample Calculation, Alfalfa Hay*

1. Identify cations and anions in %DM:

Cations: $\text{Na}^+ = 0.12\%$, $\text{K}^+ = 1.56\%$, $\text{Ca}^{+2} = 1.37\%$, $\text{Mg}^{+2} = 0.35\%$

Anions: $\text{Cl}^- = 0.44\%$, $\text{S}^{-2} = 0.28\%$, $\text{P}^{-3} = 0.24\%$

2. Set up DCAB equation:

$$[(0.12 \times 435) + (1.56 \times 256) + 0.15(1.37 \times 499) + 0.15(0.35 \times 823)] - [(0.44 \times 282) + 0.25(0.28 \times 624) + 0.5(0.24 \times 581)] \text{ mEq/100 g DM}$$

$$\text{DCAB} = 359 \text{ mEq/100 g DM}$$

Sample Calculation, Grain Mix*

1. Identify cations and anions in %DM:

Cations: $\text{Na}^+ = 0.66\%$, $\text{K}^+ = 1.14\%$, $\text{Ca}^{+2} = 1.20\%$,
 $\text{Mg}^{+2} = 0.47\%$

Anions: $\text{Cl}^- = 0.83\%$, $\text{S}^{-2} = 0.33\%$, $\text{P}^{-3} = 1.00\%$

2. Set up DCAB equation:

$$[(0.66 \times 435) + (1.14 \times 256) + 0.15(1.20 \times 499) + 0.15(0.47 \times 823)] - [(0.83 \times 282) + 0.25(0.33 \times 624) + 0.5(1.0 \times 581)] \text{ mEq/100 g DM}$$

$$\text{DCAB} = 150 \text{ mEq/100 g DM}$$

DCAB, Dietary cation-anion balance; DM, dry matter, AF, as fed.

*These values for ionic content were obtained from forage analysis and are not applicable to all feed samples. Analysis of all portions of the ration is recommended before calculation of the DCAB.

species, abnormalities in calcium homeostasis have not been identified in horses with calcium carbonate calculi, and dietary calcium restriction is not recommended. If the horse is in a metabolic state, such as mares in late gestation and early lactation, that requires a higher concentration of calcium in the diet, dietary calcium will need to be adjusted appropriately.

MUSCULOSKELETAL DISEASES

Hyperkalemic Periodic Paralysis

Dietary management for the patient with hyperkalemic periodic paralysis (HYPP) is typically instituted after a clinical episode, or after a definitive diagnosis has been reached through genetic testing (Veterinary Genetics Laboratory HYPP Testing, University of California–Davis, Davis, Calif.). Intake of high-potassium diets may precipitate an HYPP attack because serum potassium will be redistributed into muscle cells and result in cellular depolarization. Although medical management with potassium-wasting diuretics (i.e., acetazolamide and hydrochlorothiazide) is important in the long-term management of horses affected with HYPP, dietary therapy is an integral part of treatment.

Episodes of HYPP have been induced with diets that contain 1.9% and 2.9% of the diet dry matter (DM) as potassium, and current recommendations are to feed diets that contain no more than 1% potassium (DM basis). The NRC lists maintenance potassium requirements for horses at 0.4% DM, or 1.52 g/Mcal of DE/day. To achieve a level of

dietary potassium of 1% DM, a 500-kg horse could consume from 50 g to 100 g of potassium per day. It is prudent to limit the amount of potassium in the diet, but potassium should not be restricted below the maintenance requirements. The requirements for dietary potassium increase by factors of 1.1, 1.4, and 1.8 times that of maintenance requirements for horses in light, medium, and heavy work, respectively. Mares that are lactating require 1.4 times more potassium compared with maintenance, however, late-gestational requirements for potassium are approximately the same as for maintenance.

Forages vary greatly in their potassium content according to the type of soil and fertilizer used in the location where the forage is grown and the time during growth that the forage is harvested. In general young forages contain higher potassium levels whereas older forages contain less potassium. Feeds with relatively high potassium content include alfalfa hay, wheat and rice bran, molasses, brome hay, canola, and soybean meal, whereas oat hay, cereal grains (corn, oats, barley), beet pulp, and vegetable oils are lower in potassium (Table 13.4-1). Supplements that contain seaweed should be avoided. Pasture turnout is often recommended for HYPP horses to increase exercise and decrease potassium intake as only a limited amount of potassium can be obtained from fresh grass because of its high water content.

In the management of affected horses all diet changes must be made gradually (during a period of 7-10 days) because abrupt feed changes have been associated with the precipitation of HYPP episodes. Frequent, small feedings

Table 13.4-1

Mineral Content of Common Equine Feeds

Minerals (% DM)	Sodium	Potassium	Calcium	Magnesium	Sulfur	Phosphorus
Hays						
Alfalfa hay (midbloom)	0.12	1.56	1.37	0.35	0.28	0.24
Oat hay	0.18	1.49	0.32	0.29	0.23	0.25
Grass hay						
Orchardgrass	0.01	2.67	0.26	0.11	—	0.30
Bermudagrass	—	1.70	0.32	0.16	—	0.20
Concentrates						
Whole corn	0.03	0.37	0.05	0.12	0.13	0.31
Whole oats	0.07	0.42	0.11	0.19	0.22	0.34
Barley	0.02	0.58	0.05	0.14	0.16	0.38
Brans						
Wheat bran	0.06	1.37	0.14	0.63	0.24	1.27
Rice bran	0.03	1.89	0.10	0.97	0.20	1.73
Miscellaneous Feeds						
Beet pulp	0.20	0.22	0.68	0.28	0.22	0.10
Soybean meal	0.01	2.36	0.29	0.33	0.48	0.71

Modified from National Research Council (NRC): Nutrient Requirement of Horses, 5th revised edition, Washington, DC, National Academy Press, 1989.

rather than once or twice daily feeding is recommended because evidence exists that more persistent elevations in blood insulin are beneficial in the prevention of clinical episodes.

Laminitis

Nutritional intervention in cases of acute and chronic laminitis occurs concurrently with treatment of the disease. A thorough diet history will aid in the diagnosis of acute laminitis if it is related to the animal's diet. In cases of nutritionally-related laminitis, such as carbohydrate overload from excess grain, grass laminitis, or an abrupt feed change to high-energy legume hay, medical management through the administration of mineral oil or charcoal is essential to reduce the absorption of substances that may be involved in the pathogenesis of the condition. Horses with acute laminitis should be offered good-quality hay to encourage ingestion of a maintenance level of calories. Grains and grain-concentrates should be limited in the diet of a horse with acute laminitis, regardless of the cause. Owners should be counseled on measures to prevent a recurrence of nutritionally-related laminitis. Biotin supplementation with an oral dosage of 15 to 100 mg per day

for a 500-kg horse does improve hoof wall growth and may be beneficial in horses and ponies with chronic, recurrent laminitis. It should be noted that long-term (>3 months) treatment is required, and the efficacy of this treatment in horses with laminitis has not been studied. Laminitis that is related to obesity in both horses and ponies requires nutritional intervention to achieve weight loss without the induction of anorexia and hepatic lipidosis.

Supplemental Readings

- Lewis LD: Sick horse feeding and nutritional support. In Lewis LD (ed): *Equine Clinical Nutrition*, p 389, Baltimore, Williams & Wilkins, 1995.
- Meyer TS, Fedde MR, Cox JH et al: Hyperkalemic periodic paralysis in horses: a review. *Equine Vet J* 1999; 31:362-367.
- Naylor JM: Hyperkalemic periodic paralysis. *Vet Clin North Am* 1997; 13:129.
- Sloet van Oldruitenborgh-Oosterbann MM: Laminitis in the horse: a review. *Vet Q* 1999; 21:121-127.
- Wood T, Weckman TJ, Henry PA et al: Equine urine pH: normal population distributions and methods of acidification. *Equine Vet J* 1990; 22:118-121.

CHAPTER 13.5

Nutritional Therapy in Gastrointestinal Disease

MERI STRATTON-PHELPS
ANDREA J. FASCETTI
Davis, California

This chapter provides dietary recommendations for horses with selected acute and chronic gastrointestinal diseases. The nutritional management of postoperative colic patients is also discussed. Although many horses with gastrointestinal disease are able to eat, dietary modifications are often necessary to provide appropriate nutritional therapy during the recovery period. The administration of supplemental nutrition should be routine in the management of horses with disease conditions that result in hypophagia or anorexia for longer than 36 to 48 hours.

The first step in the development of a nutrition treatment plan is the calculation of the number of calories and grams of protein required for maintenance of basic metabolic functions (Box 13.5-1). The mode of nutritional support is highly dependent on the type of disease condition and the patient's appetite. In acutely ill and hypophagic

patients, it is unlikely that the entire digestible energy (DE) and protein requirement will be met only through voluntary feed consumption. However, the horse should be offered a variety of palatable feeds as a means to encourage increased food intake. If the patient is consuming less than 75% of their calculated DE requirements, then nutritional therapy using enteral (see Chapter 13.2: "Clinical Assessment of Nutritional Status and Enteral Feeding in the Acutely Ill Horse") or parenteral nutrition should be instituted.

POSTOPERATIVE COLIC SURGERY PATIENTS

Although recent improvements have been made in the medical treatment of horses recovering from colic surgery, the nutritional management of these cases has been

rather than once or twice daily feeding is recommended because evidence exists that more persistent elevations in blood insulin are beneficial in the prevention of clinical episodes.

Laminitis

Nutritional intervention in cases of acute and chronic laminitis occurs concurrently with treatment of the disease. A thorough diet history will aid in the diagnosis of acute laminitis if it is related to the animal's diet. In cases of nutritionally-related laminitis, such as carbohydrate overload from excess grain, grass laminitis, or an abrupt feed change to high-energy legume hay, medical management through the administration of mineral oil or charcoal is essential to reduce the absorption of substances that may be involved in the pathogenesis of the condition. Horses with acute laminitis should be offered good-quality hay to encourage ingestion of a maintenance level of calories. Grains and grain-concentrates should be limited in the diet of a horse with acute laminitis, regardless of the cause. Owners should be counseled on measures to prevent a recurrence of nutritionally-related laminitis. Biotin supplementation with an oral dosage of 15 to 100 mg per day

for a 500-kg horse does improve hoof wall growth and may be beneficial in horses and ponies with chronic, recurrent laminitis. It should be noted that long-term (>3 months) treatment is required, and the efficacy of this treatment in horses with laminitis has not been studied. Laminitis that is related to obesity in both horses and ponies requires nutritional intervention to achieve weight loss without the induction of anorexia and hepatic lipidosis.

Supplemental Readings

- Lewis LD: Sick horse feeding and nutritional support. In Lewis LD (ed): *Equine Clinical Nutrition*, p 389, Baltimore, Williams & Wilkins, 1995.
- Meyer TS, Fedde MR, Cox JH et al: Hyperkalemic periodic paralysis in horses: a review. *Equine Vet J* 1999; 31:362-367.
- Naylor JM: Hyperkalemic periodic paralysis. *Vet Clin North Am* 1997; 13:129.
- Sloet van Oldruitenborgh-Oosterbann MM: Laminitis in the horse: a review. *Vet Q* 1999; 21:121-127.
- Wood T, Weckman TJ, Henry PA et al: Equine urine pH: normal population distributions and methods of acidification. *Equine Vet J* 1990; 22:118-121.

CHAPTER 13.5

Nutritional Therapy in Gastrointestinal Disease

MERI STRATTON-PHELPS
ANDREA J. FASCETTI
Davis, California

This chapter provides dietary recommendations for horses with selected acute and chronic gastrointestinal diseases. The nutritional management of postoperative colic patients is also discussed. Although many horses with gastrointestinal disease are able to eat, dietary modifications are often necessary to provide appropriate nutritional therapy during the recovery period. The administration of supplemental nutrition should be routine in the management of horses with disease conditions that result in hypophagia or anorexia for longer than 36 to 48 hours.

The first step in the development of a nutrition treatment plan is the calculation of the number of calories and grams of protein required for maintenance of basic metabolic functions (Box 13.5-1). The mode of nutritional support is highly dependent on the type of disease condition and the patient's appetite. In acutely ill and hypophagic

patients, it is unlikely that the entire digestible energy (DE) and protein requirement will be met only through voluntary feed consumption. However, the horse should be offered a variety of palatable feeds as a means to encourage increased food intake. If the patient is consuming less than 75% of their calculated DE requirements, then nutritional therapy using enteral (see Chapter 13.2: "Clinical Assessment of Nutritional Status and Enteral Feeding in the Acutely Ill Horse") or parenteral nutrition should be instituted.

POSTOPERATIVE COLIC SURGERY PATIENTS

Although recent improvements have been made in the medical treatment of horses recovering from colic surgery, the nutritional management of these cases has been

BOX 13.5-1**Equations for Digestible Energy and Crude Protein Requirements in the Adult Horse**

Estimation of daily DE requirements (Mcal/day) for horses confined to a stall:

125 = 856-kg body weight

$$DE = 0.975 + 0.021 (W)$$

Estimation of daily DE requirements (Mcal/day) at maintenance levels:

200- to 600-kg body weight

$$DE = 1.4 + 0.03 (W)$$

More than 600-kg body weight

$$DE = 1.82 + 0.0383 (W) - 0.000015 (W)^2$$

Estimation of CP requirements (g/day)

Horses at maintenance levels

$$CP = (40) (Mcal \text{ of } DE/day)$$

Modified from National Research Council (NRC): Nutrient Requirement of Horses, 5th revised edition, Washington, DC, National Academy Press, 1989.

W, Weight of the horse in kilograms; DE, digestible energy; CP, crude protein.

largely overlooked. The effects of different feeding practices on postsurgical morbidity and mortality are poorly understood and no data currently exist concerning the effect of nutritional status on outcome after abdominal surgery in horses. For horses undergoing colic surgery, it is common practice to restrict feed intake for varying lengths of time. The traditional view is that early feeding after small intestinal surgery and resection or large intestinal enterotomy could exacerbate postsurgical complications including ileus, diarrhea, and impaction or leakage at the site of anastomosis. This delay in feeding leaves these horses with little to no nutritional support during the critical recovery period in the immediate postoperative period. Studies in human patients have shown that postsurgical nutritional therapy shortens recovery time and decreases complication-associated morbidity, whereas nutrient deprivation impairs wound healing and immune function. To optimize the recovery of horses undergoing colic surgery, some form of nutritional support is warranted. Horses with ileus require parenteral nutrition until the ileus is resolved and oral feed consumption meets 75% of energy needs.

Horses that have had a celiotomy performed without an enterotomy may resume oral feed intake within 12 to 24 hours after surgery if the horse has good gastrointestinal motility and does not have gastric reflux. Initially the horse can be fed small amounts of highly digestible forages including fresh grass, grass hay, or alfalfa leaves. Pelleted feeds that are finely ground can also be introduced into the

diet within the first few days after surgery. Feeds that produce more fecal bulk, such as alfalfa stems and oat hay, should be avoided for the first few days after surgery, and grains should be avoided to prevent the consumption of excess soluble carbohydrate that may disrupt intestinal bacterial flora. Early introduction of forages in the diet will provide a supplemental source of potassium and thereby help to maintain potassium homeostasis by offsetting urinary potassium loss. A gradual increase in the volume and frequency of feedings with highly digestible forages should be made if the horse tolerates the diet. However, if the horse develops signs of gastrointestinal dysfunction at any time during the recovery period, the amount of feed offered should be decreased until the resolution of signs. Grain and forages with higher fiber content can slowly be added to the ration 2 to 3 weeks after the surgery.

If both a celiotomy and an enterotomy have been performed, and the horse shows signs of normal gastrointestinal motility and a good appetite, the animal should gradually be introduced to fresh grass, or highly digestible, low bulk pelleted feeds, such as Equine Senior (Equine Senior, Purina Mills LLC, St. Louis, Mo). In these patients it is essential that small volumes of feed be offered multiple times throughout the day to avoid gastrointestinal tract distention. Although early nutritional support in these horses is important, dry forages, and grains that produce an increased volume of feces should be avoided for the first 3 to 4 weeks after surgery to lower the risk of enterotomy site complications. Horses with a poor appetite should receive enteral nutritional therapy (see Chapter 13.2: "Clinical Assessment of Nutritional Status and Enteral Feeding in the Acutely Ill Horse"). Parenteral nutrition should be used in horses that are unable to consume food orally because of gastric reflux, or patients that have ileus. In cases where gastric reflux or ileus is expected (e.g., small intestinal resection), parenteral nutrition should be started within 24 hours after completion of the surgery (see Chapter 3.9: "Parenteral Nutrition for Colic Patients").

Horses receiving either enteral or parenteral nutrition should be offered small amounts of fresh grass or pelleted feeds in order to stimulate their appetites and hasten a return to voluntary feed intake. The patient should be gradually weaned from the enteral or parenteral diet when the voluntary feed intake increases to ensure that the horse will meet at least 75% of its protein and calorie requirements after the enteral or parenteral nutrition has been discontinued. Long-term dietary modification is indicated for horses that have had more than 50% of either the small intestine or large intestine removed. In these cases a highly digestible ration is recommended for feeding over a high forage diet. In complicated cases an equine nutritionist should be consulted for the development of a suitable ration.

COLITIS

The nutritional recommendations for horses with acute large bowel diarrhea are similar regardless of the etiology and are used to complement the intensive medical management required in these cases. Daily assessment of body weight and body condition score is essential to

monitor efficacy of diet therapy. Horses with colitis of longer than 36 hours duration require dietary management as part of their treatment. If the horse is either anorexic or hypophagic, enteral feeding can be used to provide sufficient calories and protein to meet maintenance needs. Oral electrolyte solutions can be added to the enteral solution to provide supplemental electrolytes and alkalinizing substances, however, solutions that contain dextrose or glucose should be avoided to prevent complications from an osmotic diarrhea. Because enteral solutions for horses with diarrhea should contain a fiber source, human enteral formulations may be contraindicated (see Chapter 13.2: "Clinical Assessment of Nutritional Status and Enteral Feeding in the Acutely Ill Horse"). Enteral diets that contain high levels of sugar, or that have a high percentage of calories as grain, should also be avoided to prevent additional complications from osmotic diarrhea and laminitis.

Aside from enteral feeding, parenteral nutrition is another option for horses with colitis, and may be a better treatment choice in cases that are complicated by a severe protein losing enteropathy or ileus (see Chapter 3.9: "Parenteral Nutrition for Colic Patients"). Glutamine supplementation in parenteral and enteral formulations may be beneficial, although its effects have not yet been studied in horses. In some other species supplemental glutamine decreases bacterial translocation across the gastrointestinal tract, maintains the level of secretory IgA produced in the intestine, and strengthens the local intestinal immune response by serving as an energy source for lymphocytes and macrophages. Transfaunation of contents from horse feces soaked in warm saline that are administered through a nasogastric tube may help to reestablish the normal bacterial flora of the horse with colitis. Donor horse feces should not contain pathogenic *Salmonella* or *Clostridia* spp. The use of probiotics in horses with colitis is discussed elsewhere in this text (see Chapter 13.3: "Probiotics, Prebiotics, and Synbiotics").

After resolution of the diarrhea, horses with colitis must return to a regular forage-based diet. This diet should be highly digestible and should not provide excess fill to the gastrointestinal tract during the first 2 to 3 weeks of recovery to allow the tissue adequate time to heal. Even with early nutritional support, horses with colitis may lose a substantial amount of lean body mass, with a reduction in their body condition score. Once the diarrhea has resolved, supplementation of the diet with corn or soy oil may be used to increase the caloric density of the ration. Vegetable oils provide 1.6 to 1.7 Mcal per cup (200 g). If oil is incorporated into the diet, supplemental vitamin E (100 IU/100 ml of oil) should also be added. Fat supplementation should not be used in cases where intestinal fat malabsorption is suspected. It is important to make all feed changes gradually (during 7-10 days) to allow adequate time for adaptation of the horse's metabolism and intestinal bacteria to the new ration.

SAND COLIC

Sand colic can often be resolved with medical treatment, but surgical intervention is occasionally required if significant sand accumulation is present in the large intestine.

The previous recommendations for the postoperative surgery horse should be followed in surgical cases. Horses that resolve with medical treatment should be fed highly digestible forages or pelleted feed for the first 2 to 3 weeks after the sand has been passed to allow the intestinal villi time to repair from any abrasive damage that may have resulted from the presence of sand. A slow return to the horse's normal ration can be made after 2 to 3 weeks.

The most important treatment for horses with sand colic is to change their feeding management to prevent further ingestion of sand. Owners should be counseled to feed their horse in bins or in structures elevated above the ground. If the horse scatters its feed on the ground, the owner should attempt to provide some type of covering (raised palates, concrete, rubber mats) to minimize exposure to sand. Preventive therapy, including monthly treatments with psyllium hydrophilic mucilloid (psyllium), increased dietary fiber, and increased water intake may aid in the passage of previously ingested sand through alterations in gastrointestinal motility and rate of fecal passage. However, no published studies exist regarding the efficacy of these therapies for either the treatment or prevention of sand colic.

RIGHT DORSAL COLITIS

Right dorsal colitis is a localized inflammatory condition that has been associated with prolonged and/or high-dose phenylbutazone therapy. Although the prognosis is guarded to poor, some affected horses have improved with a combination of medical and nutritional management. An important goal of dietary intervention is a reduction in the mechanical and physiologic loads imposed on the large colon. Therefore complete, pelleted feeds (those that contain fiber/forage) are preferred over high forage diets, particularly poorer-quality hays. Several commercial products are available that provide adequate calories, fiber, protein, vitamins, and minerals in a highly digestible pellet. Once the energy requirements have been calculated (see Box 13.5-1), the total daily feed volume should be divided into 4 to 6 feedings. Forages, with the exception of pasture grass, should be avoided during the 3 to 6 month recovery period after a diagnosis of right dorsal colitis. If the complete pelleted ration is palatable, it may be advisable to maintain the horse on this diet even after resolution of the disease. To start the nutritional intervention, horses should be gradually changed from their normal forage ration by offering increased amounts of the pelleted feed during a 7- to 10-day period.

In addition to a complete pelleted ration, horses with right dorsal colitis may benefit from dietary supplementation with either safflower oil or corn oil ($\frac{1}{2}$ cup to 1 cup daily, divided among the feedings) and psyllium (4 oz added to the feed every 48 hours). Oil provides a concentrated source of calories (~ 1.6 - 1.7 Mcal per cup), thereby reducing the volume of pellets needed to meet the energy requirements of the horse. Safflower and corn oil contain high concentrations of linoleic acid, an arachidonic acid precursor. Supplementation with these lipids may alter the prostaglandin profile, resulting in improved mucosal healing in the colon. In some species, the metabolism of psyllium results in the production of short-chain fatty acids

that may have a beneficial effect in the healing of colonic mucosal tissue.

EQUINE GASTRIC ULCER SYNDROME

The role of diet and feeding practices in the pathogenesis of gastric ulcer disease in horses is unclear. However, it has been hypothesized that twice-daily meal feeding and diets low in fiber and high in grain promote induction of an acidic gastric environment and injury to the squamous epithelium. Furthermore, it has been speculated that the increased luminal concentrations of volatile fatty acids (VFA) that result from gastric fermentation of starches and sugars or other feedstuffs also contribute to ulcer development. This thesis is based on work in pigs that has demonstrated a relationship between gastric VFA production and squamous mucosal injury. Ulceration of the squamous mucosa has also been associated with food restriction, likely because the horse secretes gastric acid on a continual basis; therefore long periods of feed restriction result in low stomach pH.

Recent work investigating the effect of diet on gastric pH and VFA concentrations demonstrated that gastric pH in the postabsorptive state (within 5 hours after feeding) and the concentrations of acetic, propionic, and isovaleric acids were significantly higher in horses fed an alfalfa-grain diet in comparison with a bromegrass hay diet. Although gastric pH 12 hours after feeding was significantly decreased in the alfalfa-grain diet (likely caused by the twice-daily feeding protocol at 7:30 AM and 3:30 PM), both the number and severity of lesions in the nonglandular squamous mucosa were significantly decreased. Although this reduction in lesion number and severity is paradoxical in the face of higher VFA concentrations, it was postulated that the protective effect of the alfalfa-grain diet was caused by the higher protein and calcium content of this diet when compared with the bromegrass hay diet. Dietary protein can act as a buffer, and increased dietary calcium may inhibit gastric acid secretion. Although more research is required to clarify these issues, current recommendations for horses with gastric ulcers include the provision of a diet with 14% to 16% dry matter (DM) crude protein and provision of meals in small, frequent feedings. Because increased VFA production is associated with squamous mucosal injury in other species and because horses produce VFAs in their stomach, it is prudent to limit the amount of highly fermentable carbohydrates in the diet. The efficacy of dietary calcium in the prevention of gastric ulceration requires additional research before specific recommendations can be made regarding supplementation.

INFLAMMATORY BOWEL DISEASE

The long-term prognosis for horses with inflammatory bowel disease (IBD) is not usually favorable; however, nutritional support of these patients is essential to maintain their health and improve outcome from the disease. Horses with IBD demonstrate malabsorption of simple sugars after an oral glucose or xylose tolerance test and may also be hypoalbuminemic and hypoproteinemic secondary to enteric protein loss and malabsorption. Protein requirements in these patients are increased; therefore

highly digestible feeds with adequate protein (14% crude protein or greater) should be fed. If additional protein is required in the diet to prevent protein malnutrition, casein (as much as 1 lb per day) or another protein source such as soybean meal can be added to the ration. Diets that are high in digestible fiber, such as beet pulp, result in an increased production of volatile fatty acids by bacteria in the large intestine and will serve as an additional source of nutrients in the patient with IBD. Stabilized rice bran (1-2 cups, twice daily) may be beneficial because it is a source of moderately soluble fiber and fat and provides an additional source of calories. Supplemental fat, as vegetable oil, can also be added to the ration ($\frac{1}{2}$ -1 cup, once or twice daily) to increase the energy density of the diet. Addition of fat to the diet should be done gradually to ensure that gastrointestinal complications do not occur, and vitamin E (100 IU per 100 ml oil) should be supplemented to reduce damage from lipid peroxidation.

Although the addition of supplemental fat will increase the energy content of the diet, excess dietary fat is contraindicated in cases of lymphangiectasia. In addition to concerns over dietary protein and calorie adequacy, the absorption of vitamins and minerals may not be adequate to support maintenance requirements during the long-term nutritional management of horses with IBD. Regular assessment of the patient's biochemical parameters is recommended. Although horses with IBD should have their mineral status monitored, many accurate tests are invasive (i.e., liver biopsy to determine copper status), and are only recommended if a patient begins to show clinical signs of a trace mineral deficiency. Intestinal malabsorption may result in deficiencies of both fat-soluble vitamins (A, E, K) and the family of B vitamins. The reader is referred to the supplemental reading by Lewis for additional information on trace mineral and vitamin deficiency signs and testing procedures.

ENTEROLITHIASIS

Enteroliths (intestinal calculi) are composed of magnesium-ammonium-phosphate (struvite) crystals. Epidemiologic studies have identified an association between feeding both wheat bran and alfalfa and the formation of enteroliths, however, exclusion of these dietary components does not guarantee that enteroliths will not recur in an affected horse. Dietary recommendations for horses with enteroliths have been adapted from recommendations made for small animals that form urinary struvite calculi. However, the validity of this approach has not been established. Struvite calculi are susceptible to dissolution in a solution with an acidic pH (<6). Dog and cat diets designed for the prevention of struvite calculi maintain a urine pH of less than 6.5. Dietary supplementation with $\frac{1}{2}$ cup acetic acid (vinegar) at each meal reduced the colonic pH of ponies and may be beneficial in the prevention of enterolithiasis. Alternatively, dietary manipulations that use the concept of dietary cation-anion balance (DCAB; see Table 13.4-1) to achieve a diet with a low DCAB (general range of +200-300 mEq/kg diet) may also reduce the pH of the large intestinal contents and reduce enterolith formation, although this treatment has not been evaluated.

Avoidance of feeds that provide excess phosphorus and magnesium has been regarded as the best diet to prevent recurrence of enterolithiasis. Therefore bran should be avoided and alfalfa hay should be replaced in the diet by oat or grass hay. Interestingly alfalfa hay also contains a high level of cations (predominantly potassium) and has high DCAB (>400 mEq). Heavily fertilized agricultural areas often result in the growth of alfalfa hay with even higher concentrations of potassium, which could explain the regional occurrence of enteroliths in areas such as California. Conversely, both oat and grass hays have lower DCAB values (200-300 mEq) compared to alfalfa hay. Analysis of grain mixtures also gives a DCAB value within the 200 to 300 mEq range, which may contribute to the decrease in large intestinal pH observed after the introduction of grain supplementation. Evaluation of the ration using DCAB calculations (see Chapter 13.4: "Nutritional Support in Selected Metabolic, Hepatic, Urinary, and Musculoskeletal Conditions") is recommended. Because mineral content of hay varies greatly by region, soil, and growing and harvesting season, it is essential that a feed analysis be performed on all components of the diet when a low DCAB ration is formulated. Future research is needed to better define the appropriate diet for horses with enterolithiasis, but the current recommendations of a diet of grass or oat hay that is supplemented with grain and that avoids excess bran and alfalfa hay appears reasonable.

RECTAL TEARS

During the first 48 hours after a rectal tear has been sustained, the horse should not be fed, but should have access to water. The administration of mineral oil (5-10 ml/kg) in the first 1 to 2 days after a tear should facilitate passage of the colonic contents past the lesion. There-

after horses with rectal tears should be fed fresh grass or a pelleted ration that is based on ground alfalfa; long-stem fiber (hay) should not be fed. Pellets will reduce the bulk of the feces and fecal fiber length and thereby minimize trauma at the tear site. Horses can be allowed to consume fresh grass or pelleted feeds 48 hours after occurrence of the tear. The horse should be fed small amounts frequently, increasing feed volume slowly during a period of 7 to 10 days. Mineral oil, administered at 5 to 10 ml/kg once daily until the tear has almost resolved, can be mixed with the pellets or administered through a nasogastric tube if the palatability of the mineral oil/pellet slurry is poor. If needed, corn oil can be added to the diet to increase the caloric density of the pelleted feed.

Supplemental Readings

- Cohen ND, Carter GK, Mealey RH et al: Medical management of right dorsal colitis in 5 horses: a retrospective study (1987-1993). *J Vet Intern Med* 1995; 9:272-276.
- Eastman TG, Taylor TS, Hooper RN et al: Treatment of rectal tears in 85 horses presented to the Texas Veterinary Medical Center. *Equine Vet Educ* 2000; 2:342-345.
- Lewis LD: Sick horse feeding and nutritional support. In Lewis LD (ed): *Equine Clinical Nutrition*, p 389, Baltimore, Williams & Wilkins, 1995.
- Nadeau JA, Andrews FM, Mathew AG et al: Evaluation of diet as a cause of gastric ulcers in horses. *Am J Vet Res* 2000; 61:784-790.
- Schumacher J, Edwards JF, Cohen ND: Chronic idiopathic inflammatory bowel diseases of the horse. *J Vet Intern Med* 2000; 14:258-265.
- Spurlock SL, Ward MV: Parenteral nutrition. In Robinson NE (ed): *Current Therapy in Equine Medicine*, 3rd edition, p 732, Philadelphia, WB Saunders, 1992.

CHAPTER 13.6

Nutritional Management of Exertional Rhabdomyolysis

ERICA C. MCKENZIE
STEPHANIE J. VALBERG
Saint Paul, Minnesota
JOE D. PAGAN
Versailles, Kentucky

Exertional rhabdomyolysis (ER) in horses has been recognized for more than a century as a syndrome of muscle pain and cramping associated with exercise. For most of its history, it has been considered a single disease; however, in the last decade major research advances have been made in this field, providing a much greater understanding of this syndrome. Most importantly, ER comprises several different myopathies, which, despite similarities in clinical presentation, differ significantly regarding their etiopathology.

CLINICAL SIGNS AND DIFFERENTIAL DIAGNOSES

Clinical signs of ER usually occur shortly after the onset of exercise, and palpation of the lumbar and gluteal musculature frequently reveals firm and painful muscles. Excessive sweating, tachypnea, tachycardia, muscle fasciculations, and reluctance or refusal to move is seen in severe cases. The urine may become discolored as a result of the liberation of myoglobin from damaged muscle tissue. Episodes of ER vary from subclinical to severe episodes of massive muscle necrosis with recumbency and renal failure from myoglobinuria. The severity varies extensively between individuals and to some degree within the same individual. A diagnosis of ER requires establishing that serum creatine kinase (CK) and aspartate transaminase (AST) activity are above the normal range when clinical signs of muscle stiffness are present. Elevations in AST activity also may be present in asymptomatic horses with chronic exertional rhabdomyolysis.

Differential diagnoses for reluctance to move, acute recumbency, and discolored urine include lameness, colic, laminitis, pleuropneumonia, tetanus, aorto-iliac thrombosis, neurologic diseases resulting in recumbency or reluctance to move, intravascular hemolysis, and bilirubinuria. Causes of non-exercise-associated rhabdomyolysis such as infectious and immune-mediated myopathies (*Clostridium* sp., influenza, *Streptococcus equi*, *Sarcocystis* spp.), nutritional myodegeneration, traumatic or compressive myopathy, idiopathic pasture myopathy and toxic muscle damage from the ingestion of monensin, and plants including white snake root and vitamin D-stimulating species also should be considered.

ETIOLOGY AND PATHOPHYSIOLOGY

Traditionally ER was believed to be due to the accumulation of lactic acid in muscle from excessive glycogenolysis during exercise stimulated by a period of rest on a high-carbohydrate diet. No correlation exists between muscle and plasma lactate concentrations and the occurrence of ER. Most horses develop clinical signs exercising below the anaerobic threshold. Horses with rhabdomyolysis are more likely to demonstrate metabolic alkalosis if an acid-base abnormality is present.

Exertional rhabdomyolysis can be categorized into sporadic exertional rhabdomyolysis, which encompasses horses that have single or infrequent episodes of muscle necrosis with exercise; and chronic exertional rhabdomyolysis, in which affected horses have repeated episodes of rhabdomyolysis and increased muscle enzyme activity often with mild exertion.

Sporadic Exertional Rhabdomyolysis

Sporadic ER occurs commonly when a horse is exercised in excess of its level of conditioning or has its training program accelerated too quickly especially after an idle period of a few days to months. Even well-conditioned horses may sporadically develop rhabdomyolysis after exhaustive exercise. Endurance competition, especially on hot, humid days, leads to high-body temperatures, loss of fluids and electrolytes in sweat, and depletion of muscle energy stores. These losses create metabolic imbalances that lead to muscle dysfunction and damage. In some cases horses may have a higher incidence of ER after respiratory infections. Horses should not be exercised if they have a fever, acutely develop a cough, and have a nasal discharge.

Chronic Exertional Rhabdomyolysis

Chronic ER can arise from heritable myopathies such as polysaccharide storage myopathy (PSSM) or recurrent exertional rhabdomyolysis (RER). In the United Kingdom, chronic ER has been attributed to imbalances in electrolytes resulting from either low-sodium or high-phosphorus/low-calcium diets. Other causes for chronic ER likely exist but their etiopathology remains unknown.

Polysaccharide Storage Myopathy

PSSM predominantly affects Quarter Horses but also has been identified in other breeds including Paints, Appaloosas, and Morgan horses. PSSM is a glycogen storage disorder characterized by the accumulation of glycogen and abnormal polysaccharide complexes in 1% to 40% of skeletal muscle fibers. Muscle glycogen concentrations are 1.5 to 4 times greater than in normal horses. Unlike many human glycogenoses, glycogen accumulation in PSSM is not due to the inability to metabolize glycogen. Studies suggest that increased muscle glycogen is the result of enhanced insulin sensitivity and an increased rate of clearance of blood glucose as demonstrated during a carbohydrate meal, or an IV or oral glucose tolerance test. Enhanced insulin sensitivity is apparent as early as 6 months of age. Clinical signs often are elicited by a mild degree of exertion. Most commonly, rhabdomyolysis occurs in unfit horses when first put into training or after a week or more of rest. However, severe rhabdomyolysis has been observed in foals in conjunction with respiratory infections. The severity of the disease can vary greatly in individuals likely as a result of previous dietary and exercise management of the horse and potentially heterozygosity or homozygosity for the disease trait.

Frequently PSSM horses have a calm demeanor, are in good body condition, and often have a history of a change in their exercise routine such as unaccustomed stall confinement before the onset of rhabdomyolysis. Severe cases may display stiffness and reluctance to move within as little as 2 minutes of the commencement of exercise. Posturing to urinate, stretching-out, muscle fasciculations, and pawing and rolling after exercise are common with PSSM. Serum CK activity often is persistently elevated even when horses are rested for weeks. A glycogen storage disorder with histopathologic similarities to PSSM also is reported in Draft breeds and termed *equine polysaccharide storage myopathy* (EPSM). Draft horses with EPSM often have more extreme vacuolization of muscle fibers and a high percentage of fibers exhibiting atrophy on muscle biopsy. Draft horses may have the same enhanced sensitivity to insulin that PSSM Quarter Horses have shown, but this is unknown. Many of the described signs of EPSM such as normal serum CK, difficulty backing, difficulty holding up limbs for the farrier, shivers-like gait, and loss of muscle mass differ from exertional rhabdomyolysis. Recumbency and weakness accompanied by only mild elevations in serum CK and AST are also common features in Draft horses with EPSM that are not seen in Quarter Horses with PSSM. EPSM in Draft horses is reportedly responsive to dietary fat supplementation.

Recurrent Exertional Rhabdomyolysis

RER commonly afflicts Thoroughbreds and likely Standardbred and Arabian horses. In Thoroughbreds, RER has been identified as a heritable defect in intracellular calcium regulation leading to excessive muscular contraction and necrosis with exercise. The most severely affected horses are nervous young fillies in race training at the track (usually 2-year-olds). The predilection for females is not obvious in older horses with RER. Episodes of rhabdomyolysis tend to occur during training especially when horses are restrained, rather than at racing speed, and may increase in frequency as the degree of fitness increases.

Clinical episodes are often stress-induced and RER horses commonly are reported to have a nervous or extremely nervous temperament. Subclinical elevations of serum CK and AST are intermittent in nature with RER but often are found with repeated blood sampling. Rhabdomyolysis in RER horses also may occur with halothane anesthesia. Research has confirmed that although this condition is similar to malignant hyperthermia of swine and humans, also a stress-related disorder of muscle calcium regulation, the biochemical basis for the two disorders is not identical.

DIAGNOSTIC APPROACH TO CHRONIC EXERTIONAL RHABDOMYOLYSIS

Horses often are presented for evaluation because of a history of poor performance or muscle stiffness with exercise; however, at the time of evaluation, clinical evidence of rhabdomyolysis may not be present. Although clinical signs and history are often indicative of ER in many cases, a diagnosis of ER should not be made on these findings alone, and a thorough and systematic diagnostic approach is recommended to help accurately establish and address possible causative factors.

Muscle Enzyme Activity and Exercise

In horses with normal resting serum AST and CK activity but suspected to have chronic ER, a serum sample for CK activity obtained 4 to 6 hours after exercise may provide evidence for subclinical rhabdomyolysis. Submaximal exercise such as 15 minutes of trotting on a lunge line is superior to near-maximal exercise for evaluating subclinical rhabdomyolysis. Greater than a threefold to fourfold increase in the resting CK value or to more than 1000 U/L constitutes an abnormal response. Unfit horses with PSSM frequently show significant increases in muscle enzymes with light exercise and should be monitored for signs of stiffness throughout the test and exercise stopped if such signs occur. Horses with RER that are experiencing intermittent episodes of rhabdomyolysis also show abnormal elevations in CK with this test. However, if RER horses have been out of work for several weeks, they often have a normal response. The amount of exercise a horse tolerates without developing rhabdomyolysis can be used as a starting point for putting horses back into training.

Muscle Biopsy

Examination of a muscle biopsy can be helpful to distinguish PSSM from RER and to identify other disorders that contribute to clinical signs of muscle stiffness. Biopsies can be obtained from the middle gluteal muscle using a modified Bergstrom needle, at a site 8 inches along a straight line from the dorsum of the tuba coxa to the tail head. These smaller biopsies are useful if they can be frozen for histopathologic interpretation shortly after sampling. An open surgical technique to obtain a sample of semimembranosus muscle (approximately 5 inches distal to the tuber ischii) is recommended for samples that must be shipped to a laboratory for analysis. Shipped samples need to be wrapped in saline moistened gauze and kept chilled while shipped within 24 hours to a specialized laboratory.

Muscle sections prepared frozen versus formalin fixed tissue allow muscle fiber typing, mitochondrial staining, and enzymatic analyses to be performed.

In RER common histopathologic findings include a variable number of muscle fibers undergoing acute segmental necrosis, scattered muscle fibers with macrophage infiltration, a few small regenerative basophilic fibers with large central nuclei and many mature muscle fibers with centrally displaced small nuclei. PAS stains for glycogen can be dark particularly in horses in intensive training and dense deposits of glycogen can be found in subsarcolemmal locations.

Muscle biopsies from horses with PSSM often have unstained vacuoles immediately below the sarcolemma. Variable numbers of fibers undergoing necrosis and regeneration are seen. Basophilic stippling within fibers containing aggregates of abnormal polysaccharide also can be observed in hematoxylin and eosin stains. PAS staining of snap frozen sections for glycogen are often dark purple in staining intensity. Mildly affected biopsies have scattered fibers containing cytoplasmic aggregates of PAS positive polysaccharide. Grades of moderate and severe apply to biopsies that contain a high degree of subsarcolemmal vacuoles and dense-amylase resistant PAS positive inclusions in 5% to 40% of fibers. PSSM horses may not show amylase resistant PAS positive inclusions until they surpass at least 1 year of age. On average muscle glycogen concentrations are 1.5 times greater than normal but can be as high as 4 times that of normal controls. Increased PAS staining intensity alone should not be considered diagnostic of PSSM because it is subjective and varies extensively depending on the horse's diet, state of training and muscle fiber composition.

An experimental approach to identifying RER is to perform contracture tests on intercostal muscle biopsies. Small intact bundles of external intercostal muscle fibers from Thoroughbreds with RER demonstrate a lower threshold for the development of muscle contractures in response to halothane and caffeine in a muscle bath. These techniques require considerable expertise to perform and are not practical for routine application.

Urinalysis

Urinalysis test strips detect myoglobin in urine. This must be differentiated through urine cytology, serum coloration, and CBC from hemoglobin or intact red cells in the urine. Definitive tests (spectrophotometry) to confirm the presence of myoglobin rarely are indicated if a significant rise in muscle enzyme activity occurs concurrently.

Calculation of the urinary fractional excretion (FE) of electrolytes and minerals is recommended wherever it is possible that a dietary electrolyte or mineral imbalance may be initiating or exacerbating ER. A concurrent urine and serum sample should be obtained for analysis of sodium, potassium, chloride, calcium, phosphorus, and magnesium. Percent FE is calculated as follows:

$$(\text{FE}\%) (X) = \left(\frac{[\text{Cr}]_{\text{plasma}}}{[\text{Cr}]_{\text{urine}}} \times \frac{[\text{X}]_{\text{urine}}}{[\text{X}]_{\text{plasma}}} \right) \times 100$$

where Cr and X are creatinine and electrolyte or mineral concentrations, respectively, in urine or plasma.

The authors' recommendations for 95% confidence intervals for urine FE values based on noncentrifuged and acidified urine samples are presented in Table 13.6-1. Where possible, concurrent urine and serum samples at the same time each day and at the same stage of the horse's daily routine should be obtained over 3 days. The samples can be pooled or the results of the three analyses averaged because it appears that urinary electrolyte and mineral excretion may vary significantly from day-to-day within an individual despite an absence of changes in diet or routine. Therefore single samples potentially could lead to incorrect diagnosis of a dietary deficiency. Urine should not be obtained after administration of α_2 -adrenergic agonist sedatives or diuretics. Many routine chemistry laboratories use ion-specific electrodes to analyze urine electrolytes. High potassium concentrations in urine often make it difficult to obtain an accurate sodium concentration in such cases. Use of flame photometry or emission spectrophotometry can provide more accurate measurements of sodium, potassium, calcium, magnesium, and phosphorus. Where calcium, phosphorus, and magnesium are to be analyzed, samples should not be centrifuged before analysis but acidified to dissolve urine crystals. Values below the reported ranges are suggestive of conservation and possibly inadequate dietary intake that may require supplementation.

Other Tests

Serum vitamin E and plasma selenium levels should be measured to ensure that such deficiencies are not contributing to a preexisting myopathy. Recent research in PSSM horses has revealed that before 1 year of age, these animals appear to have a pronounced sensitivity to insulin compared with age-matched controls and display a significantly more rapid decline in blood glucose after insulin administration, and are more likely to become severely hypoglycemic. This response currently is being investigated as a possible method of identifying young animals with PSSM before the accumulation of abnormal polysaccharide in skeletal muscle.

NUTRITIONAL MANAGEMENT

Nutritional manipulation is emerging as a successful and convenient method of controlling ER, particularly in horses in which the administration of pharmacologic agents is frequently impossible because of racing/showing requirements. Treatment of sporadic ER is directed at

Table 13.6-1

Recommended 95% Confidence Intervals for Urine Fractional Excretion (FE) Values Based on Noncentrifuged and Acidified Urine Samples

Electrolyte	Range (% FE)	Mineral	Range (% FE)
Sodium	0.1 to 0.55	Calcium	6.0 to 15.0
Potassium	18.0 to 51.5	Phosphorus	0 to 5.0
Chloride	0.1 to 1.44	Magnesium	7.8 to 22.5

providing a well-designed exercise schedule and a nutritionally balanced diet with appropriate caloric intake and adequate vitamins and minerals.

Miscellaneous Dietary Supplements

A wide variety of dietary supplements have been used to try to ameliorate signs of chronic ER. Sodium bicarbonate traditionally has been one of the more popular supplements, but a recent study found that dietary bicarbonate does not provide any protective effects in RER horses. Thiamine, branched-chain amino acids, dimethylglycine, and lactinase have been advocated to reduce lactic acid accumulation in muscle or increase lactic acid degradation. However, because lactic acidosis is not part of the pathophysiologic processes involved in chronic ER, it is unclear how these supplements could be effective. Methylsulfonylmethane (MSM) has been used and purportedly has natural antiinflammatory effects.

Vitamin E and Selenium

Vitamin E and selenium in adequate amounts prevent the detrimental interaction of peroxides with lipid membranes of the muscle cell. Most horses with chronic rhabdomyolysis have adequate or more than adequate concentrations of vitamin E and selenium and further supplementation has not been found to have protective effects on muscle integrity in exercising horses. Supplementation of selenium should be provided only when necessary and should not be provided in excess of recommended daily amounts (0.2 to 0.3 mg per kg diet dry matter of selenium). Many feeds, particularly those designed for rhabdomyolysis, provide adequate supplementation and caution should be taken not to provide excess. Adequate vitamin E is provided in most diets by green grasses, well-cured hay, and rice bran. Additional vitamin E can be provided through dietary supplements. The diet should provide 1000 mg of vitamin E per day. Draft horses with EPSM may benefit from additional vitamin E supplementation.

Electrolytes and Minerals

Horses performing in hot and humid conditions are prone to developing electrolyte imbalances and at a minimum salt should be provided as a free choice salt lick or added to the feed at 1 to 4 ounces per day. Such climatic conditions also may warrant the addition of a commercial electrolyte mixture containing a 2:1:4 ratio of Na:K:Cl. Fresh water always should be available to horses, particularly when horses are being supplemented with electrolytes. In some horses, chronic ER has been attributed to dietary imbalances in electrolytes and minerals, particularly deficiencies of sodium, potassium, and calcium, and resolution of such imbalances may be important for managing such cases. Dietary deficiencies in electrolytes and minerals can be evaluated by ration analysis and imbalances in individual horses are best assessed by determination of urinary FE values. Although the role of magnesium deficiency in chronic ER has not been established, supplements containing magnesium have been advocated as a preventive measure. If any potential benefit exists it possibly may be due to a calming effect on behavior.

Chromium

Supplementation with oral chromium at 5 mg per day has been reported to calm horses and improve their response to exercise—measured as lower peak concentrations of insulin, cortisol, and lactic acid in exercising chromium-supplemented horses. Chromium may assist glucose and glycogen metabolism, possibly by potentiating the action of insulin. The reported calming effect of chromium may be beneficial in horses with RER because apparently stress is an important predisposing factor in this disease. However, because PSSM horses display abnormal sensitivity to insulin, chromium supplementation may be counterproductive in these horses.

Effect of Modulation of Dietary Fat and Starch

Increasing dietary fat supplementation and decreasing dietary starch has significant beneficial effects in both PSSM and RER, despite the distinct differences in the pathophysiology of these two conditions. PSSM horses have enhanced insulin sensitivity, so reducing dietary starch to a minimum decreases the postprandial rise in glucose and insulin that occurs with consumption of concentrate feeds. In PSSM, even a minor amount of fat supplementation of a low-to-moderate caloric intake provides a beneficial effect. For example, a low caloric diet fed to horses with PSSM composed of grass hay and a fat supplement (1.1 lb of rice bran) decreased skeletal muscle glycogen concentrations. The proposed mechanism for this effect is an alteration in glucose metabolism and glycogen synthesis in muscle cells. Improvement in clinical signs of muscle stiffness, however, require the addition of incrementally increasing amounts of daily exercise over 1 month.

In horses with RER the reason for the beneficial effects of fat supplementation are not thoroughly understood. In contrast to PSSM, in horses with RER fat supplementation has a significant beneficial effect only when the total caloric intake of the diet is high. RER resembles the disorder malignant hyperthermia, in which muscle necrosis occurs in genetically susceptible individuals in response to stress and excitement. High-calorie, high-starch diets are known to make horses excitable and these types of diets increase the amount of muscle damage that occurs with RER. Recent research demonstrated that RER horses fed a high-energy diet (28.8 Mcal per day) composed mostly of starch had significantly greater postexercise serum CK activity compared with one of two isocaloric lower-energy diets (21.4 Mcal per day) where calories were provided largely as either starch or as fat. In a subsequent trial postexercise serum CK activity was again significantly elevated (>3000 U/L) when horses consumed a high-starch diet (28.8 Mcal per day) but were within normal range (<400 U/L) when they consumed the same high calorie intake as a low-starch/high-fat diet (20% of the calories supplied by fat). These findings suggest that the beneficial effects of fat supplementation in RER horses could be the result of exclusion of dietary starch rather than specific protective effects of high dietary fat. In both trials RER horses had lower resting heart rates and were more tractable when consuming the high-fat diet. Given the close connection

between a nervous temperament and tying-up in RER horses, modulating anxiety and nervousness by reducing dietary starch and increasing dietary fat may decrease predisposition to RER by making these horses calmer before exercise. Studies in normal horses have demonstrated lower serum cortisol concentrations with exercise in fat-fed horses, which may be further indication of decreased psychologic stress on a fat-supplemented/low-starch diet.

Available Fat Sources

The major sources of fat available for supplementation of the equine diet are animal-based fat (tallow or lard) and vegetable-based fat, including vegetable oils and rice bran. Vegetable oil is highly unsaturated, very digestible (90% to 100%), and energy dense. Oils that can be used for supplementation include corn, soy, peanut, coconut, safflower, linseed, flaxseed, and canola. Corn oil is usually the most palatable, although soy oil also is accepted commonly. Oil is usually best mixed with the concentrate portion of the ration. Oil is energy dense and inexpensive but has the disadvantages of being messy, unpalatable to some horses, prone to rancidity in warm temperatures, and difficult to feed in large amounts. However, oil is an effective way to increase daily energy intake and may be an economical method of supplying fat to horses not requiring a large amount of supplementation. Additional vitamin E (600 to 6000 U/day) should be fed to horses receiving high-oil diets.

Animal fat is variable in digestibility (75% to 90%) and frequently cheaper than vegetable based products. However, because it is more saturated it tends to solidify at room temperature and may need to be melted for top-dressing. It also can be purchased in a more convenient powdered form. Some horses find animal fat sources unpalatable.

Rice bran and its products are palatable to most horses and contain approximately 20% fat and vitamin E. Commercial rice bran products occur as powder or an extruded pellet and are considerably more stable in warm temperatures compared with animal fat and vegetable oils. Commercial rice bran-based products are widely available and are either balanced for calcium and phosphorus or have a recommended mineral supplement that should be fed concurrently to balance the naturally high phosphorus content. Rice bran may not be appropriate for chronic exertional rhabdomyolysis because of moderate nonstructural carbohydrate (NSC) content. However, a significant fraction of the NSC portion of rice bran (approximately 6% to 8% of the NSC value) is not composed of starch and is not digested by the horse. In addition, controlled and field studies have shown that this product produces little postprandial glycemic response and feeding 1.1 to 5 lb per day of rice bran or rice bran-based products (Re-leve, Hallway Feeds, Lexington, Ky.) to both PSSM and RER horses has resulted in significant improvement in their disease.

Little information exists on the effect of different forms of fat on exertional rhabdomyolysis. A study of healthy horses found that rice bran supplying 17% DE as fat lowered heart rates and plasma lactate accumulation during exercise when compared with a compatible amount of corn oil. Rice bran-based diets also have been shown to significantly lower preexercise heart rates in RER horses, suggesting that rice bran may be an ideal component of a fat supplement for these horses.

Recommended Diets for Polysaccharide Storage

Myopathy and Recurrent Exertional Rhabdomyolysis

Feeding recommendations and several potential rations for horses with chronic exertional rhabdomyolysis are displayed in Tables 13.6-2, 13.6-3, and 13.6-4. Feeding for-

Table 13.6-2

Feeding Recommendations for Average-Size Horses (500-kg) with Chronic Exertional Rhabdomyolysis at Varying Levels of Exertion

	Maintenance	Light Exercise	Moderate Exercise	Intense Exercise
Digestible energy (Mcal/day)	16.4	20.5	24.6	32.8
% DE as NSC PSSM horses	<10	<10	<10	<10
% DE as NSC RER horses	<20	<20	<20	<20
% DE as fat PSSM horses	20	20	15-20	15-20
% DE as fat RER horses	15	15	15-20	20-25
Forage % bwt	1.5-2.0	1.5-2.0	1.5-2.0	1.5-2.0
Protein (g/day)	697	767	836	906
Calcium (g)	30	33	36	39
Phosphorus (g)	20	22	24	26
Sodium (g)	22.5	33.5	33.8	41.3
Chloride (g)	33.8	50.3	50.6	62
Potassium (g)	52.5	78.3	78.8	96.4
Selenium (mg)	1.88	2.2	2.81	3.13
Vitamin E (IU)	375	700	900	1000

DE, Digestible energy; NSC, nonstructural carbohydrate; PSSM, polysaccharide storage myopathy; RER, recurrent exertional rhabdomyolysis; bwt, body weight.

NOTE: Daily requirements derived from multiple research studies (%NSC and %fat) and the recommendations of Kentucky Equine Research, Inc., Versailles, Ky.

Table 13.6-3
Potential Rations for a 500-kg Horse with Recurrent Exertional Rhabdomyolysis

	EXERCISE		
	Light	Moderate	Intense
Forage— <i>plus</i> one of the following diets:	7 to 9 kg quality grass hay or pasture	7 to 9 kg quality grass hay or pasture	7 to 9 kg quality grass hay or 20:80 mix alfalfa/grass
Diet 1*	1 kg sweet feed + 1 kg rice bran	2 kg sweet feed + 1 kg rice bran	2.1 kg sweet feed + 1.4 kg rice bran + 1.4 kg beet pulp†
OR			5 kg Re-leve
Diet 2	1.5 kg Re-leve	3 kg Re-leve	
OR			
Diet 3*	1 kg sweet feed + 200 ml oil	2 kg sweet feed + 500 ml oil	Combination unable to achieve required DE intake

DE, Digestible energy.

Re-leve, Hallway Feeds, Lexington, Ky.

*Vitamin/mineral supplement required for nonfortified feeds. The mineral recommended for the specific rice bran product should be provided (not necessary for Re-leve).

†Soak beet pulp before feeding.

NOTE: The addition of 50 to 100 g of salt per day to all rations is recommended at increasing levels based on the level of exertion.

Table 13.6-4
Potential Rations for a 500-kg Horse with Polysaccharide Storage Myopathy

	EXERCISE		
	Light	Moderate	Intense
Forage— <i>plus</i> one of the following diets:	7 to 9 kg quality grass hay or pasture	7 to 9 kg quality grass hay or pasture	7 to 9 kg quality grass hay or 20:80 mix alfalfa/grass
Diet 1*	1.5 kg rice bran	2.25 kg rice bran	Rice bran alone unable to achieve required DE intake
Diet 2	1.5 kg Re-leve	2.5 kg Re-leve	5 kg Re-leve
Diet 3*	1.8 kg alfalfa pellets + 475 ml oil	Combination unable to achieve required DE intake	Combination unable to achieve required DE intake

DE, Digestible energy.

Re-leve, Hallway Feeds, Lexington, Ky.

*Vitamin/mineral supplement required for nonfortified feeds. The mineral recommended for the specific rice bran product should be provided (not necessary for Re-leve).

NOTE: The addition of 50 to 100 g of salt per day to all rations is recommended at increasing levels based on the level of exertion.

age at 1.5% to 2.0% of bodyweight is a fundamental part of the equine diet. The amount of dietary fat supplementation required to control exertional rhabdomyolysis is, however, controversial. Part of this controversy may arise when the two disorders PSSM and RER are not distinguished. Many PSSM horses respond to a lightly fat-supplemented, low-starch/low-calorie diet if they are exercised regularly, whereas RER horses seem to benefit only from fat supplementation when they require a high caloric intake. Thus fat does not necessarily need to supply

a minimum of 25% of the daily caloric intake for all horses with chronic ER. Feeding all horses with exertional rhabdomyolysis a minimum of 25% of the daily caloric intake as fat is not always appropriate, is difficult to achieve in the face of high caloric requirements, and may result in problems with weight gain or poorly palatable diets. The most important decision to be made for horses with PSSM and RER is what the necessary caloric intake is to maintain them at an appropriate weight and level of conditioning. Once their caloric needs are assessed, a diet

should be designed with an appropriate amount of fat and starch.

In Quarter Horse-related breeds, PSSM usually can be managed with grass hay or mixed hay (half alfalfa and half grass/oat/or brome hay) and a fat supplement that is balanced for vitamins and minerals. Starch should be decreased to less than 10% of daily digestible energy (DE) intake by eliminating grains, molasses, and corn. Rice bran can be introduced gradually into the diet as powder or as a pelleted feed. Some horses that will not eat powder consume pelleted forms of rice bran (Moorglo, Moormans, Quincy, Ill.; Re-leve, Hallway Feeds, Lexington, Ky.).

Owners must understand that eating the rice bran at a slower rate than sweet feed can be beneficial because it reduces rapid absorption of starch. Depending on the caloric requirements of the horse, 1 to 5 lb of rice bran can be fed but must be combined with a reduction in dietary starch to less than 10% of DE. An alternative source of fat is corn oil added to alfalfa pellets. An upper limit of 600 ml of oil per day is recommended and additional vitamin E should be added to the diet. Achieving the high caloric requirements for intense exercise is impossible using oil supplementation of alfalfa pellets, sweet feed, or rice bran without exceeding recommended maximum amounts of these products. To achieve the appropriate caloric intake for PSSM horses performing high-intensity exercise, high-fat/low-starch pelleted feeds designed for PSSM horses in intense exercise are recommended (see Table 13.6-2). Supplying fat at 6% to 10% by weight (or 15% to 20% of DE) of the entire ration to PSSM Quarter Horses (unless a higher energy intake is required for exercise) likely is sufficient for managing PSSM. Further benefit from more fat has not been demonstrated in controlled trials. However, none of these diets results in clinical improvement of muscle stiffness and exercise tolerance without gradually increasing the amount of daily exercise and maximizing access to turnout.

Thoroughbred horses with frequent episodes of rhabdomyolysis usually are being fed 5 to 15 lb of sweet feed/day. The incidence of subclinical rhabdomyolysis is low in Thoroughbreds being fed a moderate caloric intake whether it is in the form of sweet feed or rice bran. However, when calories are increased by the addition of more sweet feed the incidence of subclinical rhabdomyolysis is much greater. In horses with RER, one way to lower serum CK after exercise when a high-caloric intake is required is to feed a low-starch/high-fat ration. For RER horses the authors recommend feeding no greater than 20% of daily DE as nonstructural carbohydrate, and supplying 20% to 25% of daily DE from fat. The maximum recommended amount of sweet feed is 5 lb and for vegetable oil up to 600 ml/day, and rice bran up to 5 lb/day. For horses undergoing intense exercise, the combination of sweet feed and oil or sweet feed and rice bran does not achieve an adequate DE without feeding amounts of cereal grains that have been shown to elicit rhabdomyolysis in susceptible horses.

A specialized diet has been designed for horses with chronic ER in intense exercise (Re-leve) containing 13% fat by weight (rice bran and corn oil) or 20% DE as fat and only 9% DE as starch. This type of high-energy diet for RER horses may be provided through a combination of other commercially available grains, several fat supple-

ments, and highly fermentable fiber sources (soy hulls, beet pulp). Commercially available concentrates such as Strategy by Purina Mills, Vintage Racer by Blue Seal feeds, and Triple Crown Complete by Southern States Cooperative contain moderate amounts of fat (6% to 10%) and have lower NSC values (17% to 30% by weight). However, they cannot be fed in the quantities necessary to achieve the necessary calories to sustain intense exercise in RER horses without exceeding recommended NSC limits for these horses. They therefore should be combined with a fat supplement.

Expectations of Fat Supplementation

The time required for improvement in signs of exertional rhabdomyolysis is controversial. It has been suggested that a minimum of 4 months of supplementation is required and that relapses are associated primarily with disruption of supplementation. However, in the authors' experience clinical improvement with PSSM is more dependent on the amount of daily exercise and turnout than on the length or amount of dietary fat supplementation. For example, when serum CK was monitored daily postexercise, serum CK activity was almost within the normal range after 4 weeks of daily exercise, without fat supplementation. In addition, when PSSM horses were turned out 24 h/day on grass, postexercise serum CK was normal compared with high activities during the same exercise test when stall confined on a hay diet. Thus it seems that consistent fat supplementation without implementing a structured daily exercise regime in PSSM horses is likely to result in failure and confinement, whereas consuming high levels of fat is likely to lead to obesity.

Surprisingly, recent studies in RER horses show that significant reductions or normalization of postexercise serum CK activity occurs within a week of commencing a diet providing 20% DE as fat, and 9% DE as starch. This low serum CK activity compared with the high CK activity observed in the same horses on an isocaloric diet, in which 40% DE was starch, was not the result of any measurable change in muscle glycogen or metabolism during exercise. Potentially, the rapid response to decreasing starch and increasing fat was a result of neurohormonal changes that resulted in a calmer demeanor, lower preexercise heart rates, and a decreased incidence of stress-induced rhabdomyolysis. Avoiding prolonged box-stall rest in fit Thoroughbreds with RER is also important because postexercise CK activity is higher after 2 days of rest compared with values taken later in the week when performing consecutive days of the same amount of submaximal exercise. Exercise may exert beneficial effects on horses with chronic exertional rhabdomyolysis separate from the impact of reduction in dietary starch and/or fat supplementation. Failure to implement an appropriate exercise routine is very likely to lead to failure to control rhabdomyolysis.

Additional Management Strategies for Chronic Exertional Rhabdomyolysis

Daily exercise appears to be a vital adjunct for successful dietary control of PSSM. It is recommended that turnout and some exercise be started as soon as stiffness abates after an episode of rhabdomyolysis in PSSM horses, rather

than waiting for muscle enzyme activity to normalize. Serum CK activity frequently remains increased in PSSM animals that are stall rested. Severely affected horses may be able to manage only a few minutes of exercise a day, but with gradually increasing intervals of walk and 2 minutes of trot (by no more than 2 minutes per day) many of these horses are capable of eventually accomplishing intense daily exercise without clinical rhabdomyolysis. Stall confinement should be kept to a maximum of 12 hours per day, and pasture turnout is ideal.

RER horses are often fit when developing rhabdomyolysis and require only a few days off before commencing a reduced amount of training. Stall confinement should be kept to less than 24 hours if possible. Because RER appears to be a stress-related disorder, management strategies to reduce stress and excitability in these horses are important. These include turnout, exercising or feeding these horses first before other horses, providing compatible equine company, and the judicious use of low dose tranquilizers during training. Anecdotal reports of increased nervousness have been received when selenium is supplemented at higher than the recommended levels. Feeds designed for RER should be evaluated for their selenium concentrations and should not be supplemented if adequate levels are provided in the feed.

All supplemental feeds should be reduced in amount on days when energy requirements are not as high, particularly if the horse is at risk of weight gain. Other manage-

ment strategies may help to decrease the intensity of the postprandial glycemic response and include feeding small meals, providing at least 1.5% to 2.0% body weight/day in forage, and feeding a forage source either 2 hours before or concurrently with any grain. Avoiding high starch supplements such as molasses is also important.

Supplemental Readings

- Beech J: Treating and preventing chronic intermittent rhabdomyolysis. *Vet Med* 1994; 458-461.
- De La Corte FD, Valberg SJ, MacLeay JM et al: The effect of feeding a fat supplement to horses with polysaccharide storage myopathy. *World Equine Vet Rev* 1999; 4:12-19.
- Pagan JD: Carbohydrates in equine nutrition. Proceedings of the Kentucky Equine Research Equine Nutrition Conference, pp 45-50, 1997.
- Valberg SJ: Muscular causes of exercise intolerance in horses. *Vet Clin North Am Equine Pract* 1996; 12:495-515.
- Valberg SJ, MacLeay JM, Mickelson JR: Exertional rhabdomyolysis and polysaccharide storage myopathy in horses. *Comp Cont Educ Pract Vet* 1997; 19:1077-1086.
- Valberg SJ, Mickelson JR, Gallant EM et al: Exertional rhabdomyolysis in Quarter horses and Thoroughbreds: one syndrome, multiple aetiologies. *Equine Exercise Physiology 5: Equine Vet J Suppl* 1999; 30:533-538.
- Valentine BA, Van Saun RJ, Thompson KN et al: Role of dietary carbohydrate and fat in horses with equine polysaccharide storage myopathy. *J Am Vet Med Assoc* 2001; 219:1537-1544.

SECTION XIV

Neurologic Disease

Edited by Dr. Robert J. MacKay

CHAPTER 14.1

Limb Weakness, Atrophy, and Other Signs of Peripheral Nerve Disease

LINDA L. BLYTHE
Corvallis, Oregon

Peripheral neuropathies are characterized by damage or disease of either or both of the motor and sensory nerves that supply the thoracic and pelvic limbs in addition to those to the neck, body and tail, bladder, and rectum. However, dysfunction of those peripheral nerves that supply the limbs with both sensory and motor function constitutes most of the clinical cases. With these, the most common clinical signs are lameness or gait abnormalities. Motor nerves have their neuronal cell bodies in the ventral horn of the spinal cord with axons exiting through the ventral root and being distributed in the peripheral nerves to the muscles. This motor unit includes the neuromuscular junction, which is affected in cases of botulism. Dysfunction of any part of the motor unit is termed *lower motor neuron disease* and can be of spinal cord origin or arising from damage to one or more of the peripheral nerves. Most peripheral neuropathies involve one or more nerves to a single limb with both motor and sensory losses discernable to specific nerves. But diseases such as polyneuritis equi (cauda equina neuritis), botulism, and stringhalt can affect the nerves to multiple limbs and be confused with spinal cord problems such as equine protozoal myeloencephalopathy (EPM) or equine motor neuron disease. In their examination, veterinarians should try to localize the nerve damage as arising from either the spinal cord or from the peripheral nerves because this will influence their list of differential diagnoses.

CLINICAL DIAGNOSTIC WORK-UP

Gait Analysis

Initially, clinical signs of peripheral neuropathies can range in presentation from obscure lameness to sudden onset of an inability to bear weight or ambulate on a limb. With the

former, veterinarians most often begin to suspect a neuropathy when the results of a lameness examination that include the standard work-up of gait analysis, joint flexion and extension, selective nerve blocks, and radiography indicate no abnormalities to account for the lameness. With an acute onset of lameness, dragging or misplacing a limb, or inability to bear weight on a limb, the neurologic examination must focus on determination of which muscle groups are affected and what sensory losses are present. The horse should be observed at a walk as it moves toward and away from examiner and from side to side, going both directions. In the former, if abduction of the shoulder joint away from the body wall during the weight-bearing phase were the only abnormality, this would indicate suprascapular nerve damage. Dropping of the hip during the weight-bearing phase would indicate damage to quadriceps muscle group innervated by the femoral nerve or the muscles innervated by the ischiatic nerve.

During the gait analysis, the veterinarian should observe the horse's ability to flex the elbow and extend the carpus and the digit. Inability or reduction of elbow joint flexion indicates damage to the musculocutaneous nerve, which innervates the biceps brachii and the brachialis muscles. Inability to advance the knee or extend the hoof would indicate radial nerve damage. Inability to bear weight on the thoracic limb in a standing position indicates loss of radial nerve innervation to the triceps muscle group. In a similar manner, the ability to stand on the pelvic limb requires that the femoral nerve function be intact. A dropped or overflexed hock indicates tibial nerve damage, whereas the inability to extend the hind foot or place it squarely on the ground while standing or walking indicates fibular (peroneal) nerve damage.

Sensory Nerve Evaluation

Sensory evaluation of the limb in acute injuries is valuable in determination of which nerves may be affected and as a prognostic indicator of the severity of the damage. Even if a fracture is found, the veterinary professional should still evaluate the cutaneous responses to touch and pain to determine if the adjacent nerves are intact and functioning or possibly damaged or severed. When a peripheral nerve suffers compressive damage from trauma or subsequent edema of itself or the surrounding tissues, the myelinated nerve fibers with the largest diameter are the first to be affected. Clinically, the order of loss of testable functions is as follows: first proprioceptive fibers that allow the horse to know where its limb is relative to space are lost. This would result in visible ataxia or inappropriate placement of the limb. Second, the large myelinated motor axons are compromised, and paresis or paralysis of voluntary and reflex movements occurs. Third, the loss of the next smaller axons occurs, which carry cutaneous and deep mechanoreceptor sensory information to the central nervous system. The loss of these fibers is identified when an animal does not appear to perceive or respond to touch of its skin. Last to be lost are the smallest diameter fibers, those that carry pain stimuli to the spinal cord and brain. Thus the prognosis becomes more serious as clinical signs in a horse progress from loss of proprioception, to loss of motor function, to the loss of perception and response to touch, followed finally by the inability to feel and react to painful stimuli.

Loss of proprioception and motor weakness are evaluated by watching the horse move at a walk, turning in tight circles, moving over obstacles, and backing. Sway tests, in which one person leads a horse at the walk and another person pulls on the tail while walking forward, are useful in detecting both ataxia and motor weakness. The ability of the horse to perceive touch is best evaluated by gently touching various parts of the skin with a sharp pencil. Horses are sensitive to this type of stimulus and reliably move the skin and/or underlying muscles. If touch sensation is lost, then the veterinary professional can map the extent of sensory loss by systematically touching the skin from front to back with a pencil at 2-cm intervals, starting at the shoulder area and working distally down the limb. When an area of skin that has a loss of response to the pencil touch is found, then the veterinarian can outline the total sensory loss by placing a spot of white poster paint or a black felt tip pen mark at the junction of the desensitized and sensitive skin (Figure 14.1-1). To do this takes only a few minutes and allows the identification of affected nerves using the sensory innervation maps below. Once this area of sensory loss to touch has been outlined, it should be evaluated in a similar manner for response to pain by pinching the skin at 2-cm intervals with hemostats. Loss of pain in all or part of the mapped area indicates either severe damage or severance.

Innervation of the cutaneous areas of the thoracic and pelvic limbs of the horse has been mapped using neuro-



Figure 14.1-1 **A**, Hackney pony presented with acute onset of a “dropped elbow” in the right forelimb. A musculoskeletal examination, including nerve blocks, radiographs, and a shoulder joint tap, was negative for any abnormalities. Evaluation of the perception of touch was done with a sharp No. 2 pencil. Areas enclosed by the white poster paint were insensitive to touch but still responded to a painful pinch with a hemostat. This would indicate damage to the axillary, radial, and musculocutaneous nerves. **B**, Pony seen in **A** after 9 days of antiinflammatory therapy. The cutaneous area not responsive to touch had decreased in size. Several days later this horse had no sensory deficits and had begun to show markedly improved motor function and strength.

physiologic methodology and is seen in Figures 14.1-2 and 14.1-3. Figure 14.1-2 illustrates the extent of innervation of each of the main sensory nerves that supply the limb. There is extensive overlap of cutaneous innervation in many areas of the limbs. Clinically, loss of either touch or pain sensation from these areas with multiple peripheral nerve supply indicates that multiple nerves are involved. For example, if three nerves supply an area of skin and one is lost, it is not possible to detect any sensory loss to touch or pain in the area. However, if two or three nerves are not functioning, then touch and pain are not perceived. Figure 14.1-3 illustrates those areas of skin that have a single nerve supply (autonomous zones). Knowledge of these areas allows testing of the function of the individual nerves.

When traumatic injury to a limb and its peripheral nerves does not involve the skeletal system, these horses may have lost both proprioceptive and motor function but still have the ability to perceive and react to touch and pain over the entire limb. This indicates that the nerves are intact. The prognosis is good with immediate treatment directed at reducing edema and inflammation (see below). Another horse may have loss of proprioception, paresis, or paralysis of a limb and the inability to perceive touch, but it retains its ability to perceive pain (see Figure 14.1-1). This indicates a more severe injury, but the affected peripheral nerve(s) are still intact and the prognosis is good with treatment. When loss of pain is found with all the aforementioned deficits in the acute injury case,

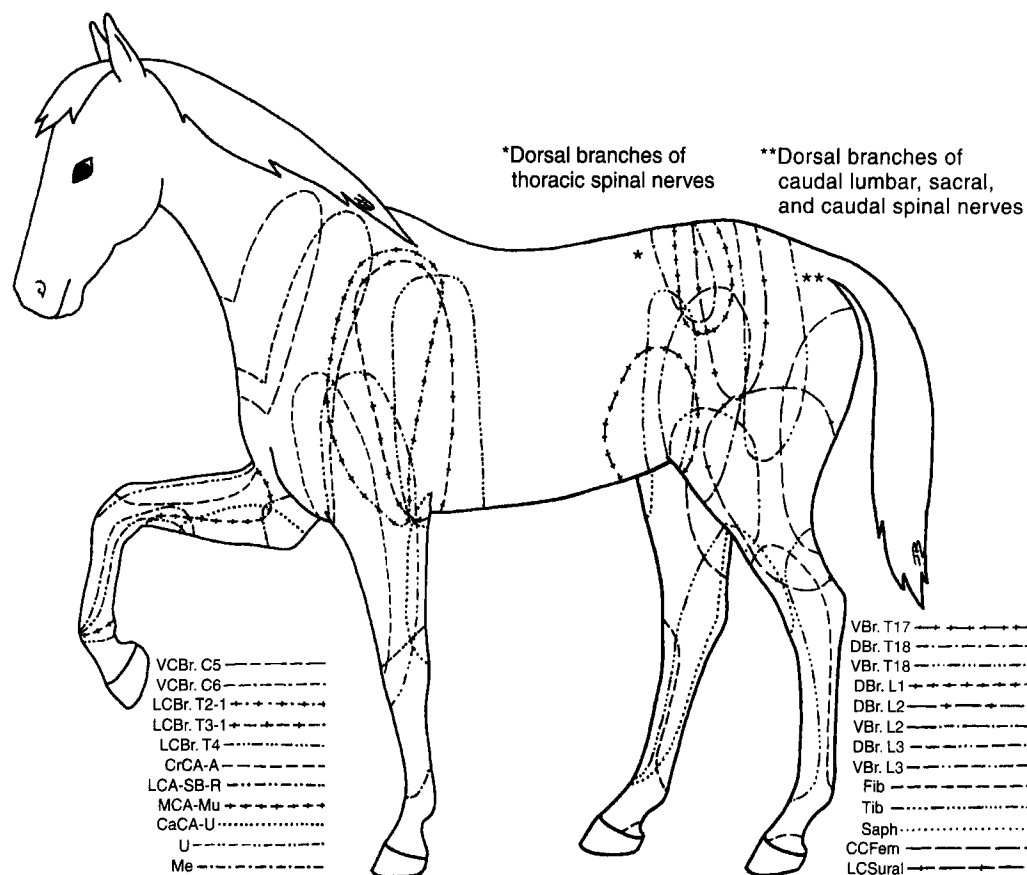


Figure 14.1-2 Sensory cutaneous areas of the pectoral and thoracic limb regions of the horse: *VCBr, C5*, Ventral cutaneous branch of cervical spinal nerve 5; *VCBr, C6*, ventral cutaneous branch of cervical spinal nerve 6; *LCBr, T2-1*, lateral cutaneous branch of thoracic spinal nerve 2 (part of intercostobrachial nerve); *LCBr, T3-1*, lateral cutaneous branch of thoracic spinal nerve 3 (part of intercostobrachial nerve); *LCBr, T4*, lateral cutaneous branch of thoracic spinal nerve 4; *CrCA-A*, cranial cutaneous antebrachial nerve of the axillary nerve; *LCA-SB-R*, lateral cutaneous antebrachial nerve of the superficial branch of the radial nerve; *MCA-Mu*, medial cutaneous antebrachial nerve of the musculocutaneous nerve; *CaCA-U*, caudal cutaneous antebrachial nerve of the ulnar nerve; *U*, ulnar nerve; *Me*, median nerve.

Sensory cutaneous areas of the thoracolumbosacral regions and the pelvic limb: *VBr, T17*, Ventral branch of thoracic spinal nerve 17; *DBr, T18*, dorsal branch of thoracic spinal nerve 18; *VBr, T18*, ventral branch of thoracic spinal nerve 18; *DBr, L1*, dorsal branch of lumbar spinal nerve 1; *DBr, L2*, dorsal branch of lumbar spinal nerve 2; *VBr, L2*, ventral branch of lumbar spinal nerve 2; *DBr, L3*, dorsal branch of lumbar spinal nerve 3; *VBr, L3*, ventral branch of lumbar spinal nerve 3; *Fib*, fibular (peroneal) nerve; *Tib*, tibial nerve; *Saph*, saphenous nerve; *CCFem*, caudal cutaneous femoral nerve; *LCSural*, lateral cutaneous sural nerve.

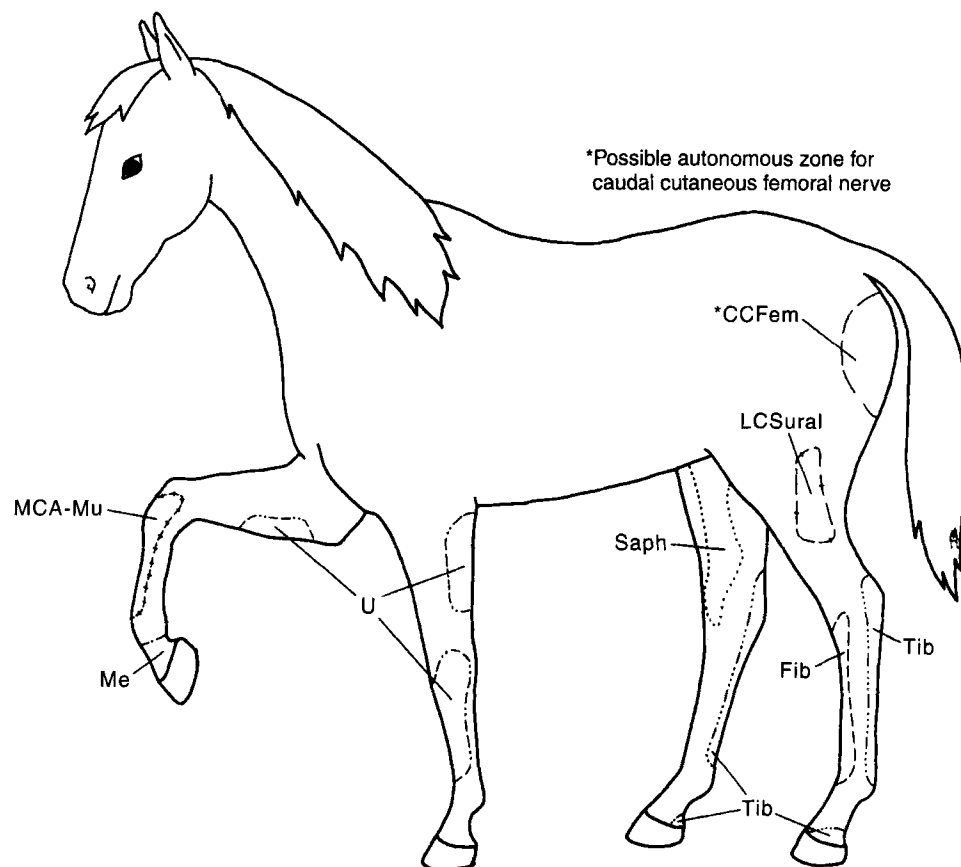


Figure 14.1-3 Autonomous zones of innervation in the horse. *CCFem*, Caudal cutaneous femoral nerve; *LCSural*, lateral cutaneous sural nerve; *MCA-Mu*, medial cutaneous antebrachial nerve of the musculocutaneous nerve; *Me*, median nerve; *U*, ulnar nerve; *Saph*, saphenous nerve; *Tib*, tibial nerve; *Fib*, fibular (peroneal) nerve.

the prognosis becomes considerably more guarded. At this point, the veterinary professional does not know whether the peripheral nerve or nerves are severed or whether they are simply severely swollen. Quick institution of aggressive antiinflammatory measures is warranted in addition to daily monitoring of the cutaneous responses to touch and pain.

If the nerve(s) is intact, then recovery of its function will return in the reverse order of loss: that is, pain perception will return first, followed by perception of touch, and then motor strength. Proprioception will be the last sensory function to return. Loss of pain that persists past 7 days indicates a guarded prognosis for a 2- to 3-week return to function with medical therapy. In these cases either the nerve(s) may be severed and have to be surgically repaired or the axons may have been damaged severely enough to undergo degeneration and loss of the distal segment (Wallerian degeneration). In these latter cases, the nerve attempts to regrow at a clinically estimated rate of 1 mm per day (1 inch per month). Within 2 weeks of total denervation, a muscle loses approximately one half of its muscle mass. Neurogenic atrophy continues until the muscle is reinnervated. If the muscle that needs to be reinnervated is within 12 inches of the

regenerating nerve and if scar tissue does not impede the axonal regrowth, then reinnervation and return of muscle size and function is possible within those time constraints. As a general rule, muscles that are denervated totally must receive reinnervation before 12 months or they will be permanently replaced by fibrosis and fat tissue.

In progressive peripheral neuropathies or 2 weeks after an acute injury or in chronic cases, identification of those muscles that have undergone partial or total neurogenic atrophy can be used as additional information with which to identify the damaged peripheral nerves. Table 1 on p. 316 of the fourth edition of *Current Therapy in Equine Medicine* presents the primary innervation of the major muscles of the limbs of the horse.

In all cases, a complete neurologic examination is warranted to determine the presence and/or extent of any reflex losses. These losses may include cutaneous trunci, anal sphincter, tail tone, and limb muscle tone or possible brain involvement as detected by cranial nerve deficits and disorder of mentation. In addition, the loss of one or more reflexes allows the veterinarian to localize readily the problem to specific peripheral nerves or spinal cord segments in that reflex arc.

NEURODIAGNOSTIC EVALUATION

Electromyography

When muscle atrophy may be a result of either disuse atrophy or partial nerve loss, electromyography may be a useful tool to differentiate between them. Denervated muscles after 5 days have abnormal electrical potentials (fibrillation potentials and positive sharp waves) detected in resting muscles. Muscles with disuse atrophy do not have these electrical abnormalities. Portable electromyography (EMG) machines are becoming more common in large equine clinics and veterinary teaching hospitals. This instrument is basically a voltmeter that allows detection of abnormal electrical potentials from damaged or denervated muscles. Using a coaxial needle (a needle within a needle), the operator inserts the needle into the various muscles and listens for the characteristic sounds of denervation, that is, fibrillation potentials and positive sharp waves. These spontaneous electrical discharges also are displayed on an oscilloscope.

Although EMG abnormalities are also present in some myopathies, these usually can be differentiated from neuropathies in that most myopathies have muscles painful to palpation, a stiff gait or reluctance to move at all and by elevated serum muscle enzymes. EMG abnormalities in suspected traumatic nerve injuries are useful in determination of the extent of nerve damage. When EMG abnormalities are found in muscles of multiple limbs or in the head, this would indicate a diffuse neurologic disease process such as equine EPM, equine motor neuron disease, cauda equina neuritis (polyneuritis equi), or botulism or a myopathy such as equine polysaccharide storage myopathy (see Valentine in readings list).

Nerve Conduction Velocity Measurements

Nerve conduction velocity is a precise method of testing the integrity of a nerve. These measurements test the rate of action potential conduction down the largest, most heavily myelinated axons. With pressure or edema, it is the myelin on these large axons that is first to be damaged, which results in a slowing or absence of the nerve conduction. Techniques for doing either sensory nerve conduction velocity (see Blythe in readings list) or motor nerve conduction velocity (see Henry in readings list) or normal values have been published. The newer EMG instruments have the capabilities of making these measurements. However, these tests usually are performed only in referral veterinary hospitals because the measurements require precise placement of the stimulating and recording electrodes and because general anesthesia usually is required. Their value in differentiating different neuropathies has not been documented. Similarly, the use of magnetic resonance imaging (MRI) is available in some universities for horses and may prove to be useful in complicated cases of neuropathy such as differentiating causes of brachial plexus dysfunction.

DIFFERENTIAL DIAGNOSIS AND TREATMENT

The most common peripheral neuropathies are caused by trauma. In the forelimb, the most common are suprascapular nerve damage ("sweeny") and brachial plexus

paresis or paralysis. In the suprascapular neuropathy, the damage may be a result of direct trauma to the nerve passing around the distal scapula near the shoulder joint. Both suprascapular nerve and brachial plexus injury may be the result of an overstretching or tearing of the nerves when a horse slips or falls; the latter can damage the brachial plexus. In any acute trauma to the peripheral nerves of the limbs, treatment should be directed to reducing inflammation. Resolution of inflammation allows for reduction of damage as a result of edema or pressure and allows for remyelination in 1 to 2 weeks.

Cold water therapy, stall confinement, and nonsteroidal antiinflammatory drugs such as phenylbutazone (4 mg/kg q12h) or flunixin meglumine (1.1 mg/kg IM, IV, or PO q24h or divided q12h), corticosteroids such as dexamethasone (0.05 mg/kg IV or IM q12h), and dimethyl sulfoxide (1 g/kg IV in a 10% solution or via stomach tube q12-24h or topical if the nerves are subcutaneous) may be used to reduce inflammation for the initial 2 to 3 days. Trauma to the hindlimb may result in stringhalt-type gait (repeated hyperflexion of the limb during initial phases of movement) if the distal extensor muscles are damaged. Because this is seen more as a chronic result of the damage, correction often involves a surgical transection of the lateral digital extensor tendon. Other causes of the stringhalt-type of signs include ingestion of *Hypochoeris radicata* (flatweed) or other toxic plants, and EPM. Surgical decompression may also be the treatment of choice with suprascapular nerve paralysis that does not resolve within 2 months (see McIlwraith in readings list).

The second most common cause of a lower motor neuron disease that can appear to be a focal or diffuse peripheral neuropathy is EPM (see Chapter 2.11: "Equine Protozoal Myeloencephalopathy"). Horses with this condition present most often as a symmetric or asymmetric spinal cord lesion, but lameness and/or muscle atrophy are often the first clinical signs noted in these cases. Less common is polyneuritis equi (cauda equina neuritis, see Chapter 14.6: "Bladder, Rectal, Anal, and Tail Paralysis; Perineal Hypalgnesia; and Other Signs of Cauda Equina Syndrome"), which is an idiopathic syndrome with multiple possible etiologies that affect the spinal cord and nerve roots including the cranial nerves. Although trauma to the cauda equina may be the most common cause, an autoimmune-based etiology also may account for some of the cases. The latter is usually a slowly progressive neuropathy. The initial clinical signs may be an obscure lameness with some muscle atrophy of the pelvic limbs and tail. Loss of tail tone and anal sphincter and bladder dysfunction resulting from pelvic nerve dysfunction place this disease high on the list of differential diagnoses. Treatment is not effective.

Equine motor neuron disease is a rare diffuse lower motor neuron disease associated with chronic vitamin E deficiency as a predisposing factor. It affects the nerve cell bodies throughout the spinal cord and is characterized by muscle weakness, tremors, and atrophy. Treatment with vitamin E may prevent progression of the disease, but full return to function is uncommon.

Postanesthetic neuropathies most commonly affect the radial nerve in the forelimb or the fibular (peroneal) nerve in the pelvic limb. Proper padding of the limbs while the horse is in lateral recumbency and maintenance of blood

pressure with fluids during anesthesia help prevent such pressure or ischemic injuries to these nerves. Post foaling obturator nerve paralysis is an infrequent sequela and may occur without any evidence of dystocia. Clinical signs range from abduction and circumduction of the pelvic limbs to paraplegia. Treatment is aimed at reduction of inflammation, stall confinement on non-slippery surface, and good nursing care if the horse is paretic or paralyzed. Support with a sling, if tolerated, may help reduce the complications of prolonged recumbency. Prognosis has been reported to be fair, with about 50% recovering (see Hahn in readings list).

Botulism is a disease of the neuromuscular junction caused by the exotoxin of *Clostridium botulinum*. The toxin interferes with the release of acetylcholine in the presynaptic ending of motor nerves resulting in motor weakness to paralysis. Clinical signs of a flaccid paresis to paralysis affecting all four limbs with loss of withdrawal and other reflexes including tail, limb muscle, tongue, and eyelid tone in an alert horse are indicative of this intoxication. The gait may be stilted and the horse may have a shortened stride with muscle tremors evident in the large triceps and quadriceps muscle groups. In foals, it is described clinically as the *shaker foal syndrome* because of the muscle weakness. The pathogenesis, diagnosis, and treatment are discussed elsewhere.

Neuromas are peripheral nerve problems, most com-

monly seen as a complication in elective postsurgical transactions of the palmar or plantar nerves. Diagnosis is based on history and evidence of a painful mass at the surgical site several weeks after the surgery. Surgical removal is usually required for correction of the problem and recurrences may occur because the formation of a neuroma is a natural reparative process of the distal axons.

Supplemental Readings

- Blythe LL, Engel HN, Rowe KE: Comparison of sensory nerve conduction velocities in horses versus ponies. *Am J Vet Res* 1988; 49:2138-2142.
- Hahn CN, Mayhew IG, MacKay RJ: Diseases of the peripheral (spinal) nerves. In Colahan PT, Mayhew IG, Merritt AM et al (eds): *Equine Medicine and Surgery*, 5th edition, St Louis, Mosby, 1999.
- Henry RW, Diesem CD: Proximal equine radial and median motor nerve conduction velocity. *Am J Vet Res* 1981; 42:1819-1822.
- McIlwraith CW, Robertson IT: Decompression of the suprascapular nerve. In McIlwraith CW, Robertson J (eds): *Equine Surgery: Advanced Techniques*, Baltimore, Williams & Wilkins, 1998.
- Valentine BA, Van Saun RJ, Thompson KN, Hintz HF: Role of dietary carbohydrate and fat in horses with equine polysaccharide storage myopathy. *J Am Vet Med Assoc* 2001; 21:1537-1544.

CHAPTER 14.2

Diffuse Skeletal Muscle Weakness (Myasthenia)

BRUCE C. MCGORUM

Edinburgh, Scotland

This chapter describes the diagnosis and management of disorders that cause diffuse, symmetric weakness of skeletal muscles (myasthenia; Table 14.2-1). This sign reflects dysfunction of the motor unit, which comprises lower motor neurons (central nerve cell bodies and peripheral nerve axons), neuromuscular junctions, and skeletal muscles. This section excludes disorders that cause myasthenia that is focal, such as that caused by peripheral nerve injury, multifocal (e.g., equine protozoal myeloencephalitis), or confined solely to the hindlimbs (e.g., aortoiliac thrombosis).

ETIOLOGY AND PATHOGENESIS

The reader is directed to previous editions of *Current Therapy in Equine Medicine* (CTEM) for detailed information on the etiopathogenesis of equine motor neuron disease (EMND; CTEM4, p. 321), botulism (CTEM4, p. 326), hyperkalemic

periodic paresis (HYPP; CTEM3, p. 117), postanesthetic myopathy (CTEM4, p. 124), equine rhabdomyolysis syndrome (ERS; CTEM4, p. 115), ionophore toxicity (CTEM3, p. 366), and equine grass sickness (EGS; CTEM4, p. 203).

The idiopathic postanesthetic myasthenia syndrome has been observed in 3 horses after general anesthesia. This may represent a form of botulism or a drug-induced neuromuscular dysfunction. Proposed contributory factors include administration of aminoglycosides or tetracyclines, in conjunction with halothane anesthesia and depolarizing agents.

Tick paralysis is a dysfunction of the neuromuscular junction caused by a toxin present in saliva from several species of ticks, including *Ixodes holocyclus* and *Dermacentor andersoni*. Because the effect of the toxin is dose dependent, only foals are affected.

Myasthenia gravis is an immune mediated disorder in which auto-antibodies directed against the motor end

pressure with fluids during anesthesia help prevent such pressure or ischemic injuries to these nerves. Post foaling obturator nerve paralysis is an infrequent sequela and may occur without any evidence of dystocia. Clinical signs range from abduction and circumduction of the pelvic limbs to paraplegia. Treatment is aimed at reduction of inflammation, stall confinement on non-slippery surface, and good nursing care if the horse is paretic or paralyzed. Support with a sling, if tolerated, may help reduce the complications of prolonged recumbency. Prognosis has been reported to be fair, with about 50% recovering (see Hahn in readings list).

Botulism is a disease of the neuromuscular junction caused by the exotoxin of *Clostridium botulinum*. The toxin interferes with the release of acetylcholine in the presynaptic ending of motor nerves resulting in motor weakness to paralysis. Clinical signs of a flaccid paresis to paralysis affecting all four limbs with loss of withdrawal and other reflexes including tail, limb muscle, tongue, and eyelid tone in an alert horse are indicative of this intoxication. The gait may be stilted and the horse may have a shortened stride with muscle tremors evident in the large triceps and quadriceps muscle groups. In foals, it is described clinically as the *shaker foal syndrome* because of the muscle weakness. The pathogenesis, diagnosis, and treatment are discussed elsewhere.

Neuromas are peripheral nerve problems, most com-

monly seen as a complication in elective postsurgical transactions of the palmar or plantar nerves. Diagnosis is based on history and evidence of a painful mass at the surgical site several weeks after the surgery. Surgical removal is usually required for correction of the problem and recurrences may occur because the formation of a neuroma is a natural reparative process of the distal axons.

Supplemental Readings

- Blythe LL, Engel HN, Rowe KE: Comparison of sensory nerve conduction velocities in horses versus ponies. *Am J Vet Res* 1988; 49:2138-2142.
- Hahn CN, Mayhew IG, MacKay RJ: Diseases of the peripheral (spinal) nerves. In Colahan PT, Mayhew IG, Merritt AM et al (eds): *Equine Medicine and Surgery*, 5th edition, St Louis, Mosby, 1999.
- Henry RW, Diesem CD: Proximal equine radial and median motor nerve conduction velocity. *Am J Vet Res* 1981; 42:1819-1822.
- McIlwraith CW, Robertson IT: Decompression of the suprascapular nerve. In McIlwraith CW, Robertson J (eds): *Equine Surgery: Advanced Techniques*, Baltimore, Williams & Wilkins, 1998.
- Valentine BA, Van Saun RJ, Thompson KN, Hintz HF: Role of dietary carbohydrate and fat in horses with equine polysaccharide storage myopathy. *J Am Vet Med Assoc* 2001; 21:1537-1544.

CHAPTER 14.2

Diffuse Skeletal Muscle Weakness (Myasthenia)

BRUCE C. MCGORUM

Edinburgh, Scotland

This chapter describes the diagnosis and management of disorders that cause diffuse, symmetric weakness of skeletal muscles (myasthenia; Table 14.2-1). This sign reflects dysfunction of the motor unit, which comprises lower motor neurons (central nerve cell bodies and peripheral nerve axons), neuromuscular junctions, and skeletal muscles. This section excludes disorders that cause myasthenia that is focal, such as that caused by peripheral nerve injury, multifocal (e.g., equine protozoal myeloencephalitis), or confined solely to the hindlimbs (e.g., aortoiliac thrombosis).

ETIOLOGY AND PATHOGENESIS

The reader is directed to previous editions of *Current Therapy in Equine Medicine* (CTEM) for detailed information on the etiopathogenesis of equine motor neuron disease (EMND; CTEM4, p. 321), botulism (CTEM4, p. 326), hyperkalemic

periodic paresis (HYPP; CTEM3, p. 117), postanesthetic myopathy (CTEM4, p. 124), equine rhabdomyolysis syndrome (ERS; CTEM4, p. 115), ionophore toxicity (CTEM3, p. 366), and equine grass sickness (EGS; CTEM4, p. 203).

The idiopathic postanesthetic myasthenia syndrome has been observed in 3 horses after general anesthesia. This may represent a form of botulism or a drug-induced neuromuscular dysfunction. Proposed contributory factors include administration of aminoglycosides or tetracyclines, in conjunction with halothane anesthesia and depolarizing agents.

Tick paralysis is a dysfunction of the neuromuscular junction caused by a toxin present in saliva from several species of ticks, including *Ixodes holocyclus* and *Dermacentor andersoni*. Because the effect of the toxin is dose dependent, only foals are affected.

Myasthenia gravis is an immune mediated disorder in which auto-antibodies directed against the motor end

Table 14.2-1

Disorders that Cause Diffuse Skeletal Muscle Weakness and the Muscle Groups Predominantly Affected

Disorder	Muscles Affected
Lower Motor Neuron Disorders	
Equine motor neuron disease (EMND)	Type I myofibers; postural muscles of body, limbs, and neck; sacro-caudalis dorsalis medialis; muscles innervated by cranial nerves V, VII, and XII affected subclinically
Neuromuscular Junction Disorders	
Botulism	Generalized weakness of skeletal muscles; variable involvement of smooth muscles
Postanesthetic myasthenia syndrome	Generalized weakness of skeletal muscles
Tick paralysis	Generalized weakness of skeletal muscles
Myasthenia gravis	Generalized weakness of skeletal muscles
Primary Muscle Disorders	
Hyperkalemic periodic paresis (HYPP)	Facial, tongue, pharyngeal, laryngeal, limb, and neck muscles
Generalized postanesthetic myopathy	Type II > Type I myofibers; muscles of the back, hindlimb, shoulder, and trunk
Severe equine rhabdomyolysis syndrome (ERS)	Type II > Type I myofibers; back, hindlimb, and shoulder muscles
Atypical myoglobinuria	Limb, neck, intercostals, diaphragm, and cardiac muscles
Nutritional myodegeneration	Types I and IIA myofibers; limb, neck, tongue, masticatory, pharynx, intercostal, diaphragm, and cardiac muscles
Ionophore toxicity	Myocardium, diaphragm, and skeletal muscles
Pathophysiology of Muscle Weakness Unknown	
Equine grass sickness (EGS)	Weakness of skeletal muscles of neck, trunk, and limbs; predominant clinical features reflect weakness of smooth muscles because of dysfunction of autonomic and enteric neurons

plate cause neuromuscular dysfunction. Three horses have shown signs consistent with this disease, of which one had detectable auto-antibodies (IG Mayhew, personal communication, Edinburgh, Scotland, 2002).

Atypical myoglobinuria is characterized by diffuse skeletal myodegeneration. It probably is caused by ingestion of an unidentified pasture-derived toxin. In contrast to ERS, outbreaks may occur, and it typically affects horses and ponies that are grazing poor quality pasture, with no supplementary feeding and no exercise.

Nutritional myodegeneration or white muscle disease is an oxidative myonecrosis that affects primarily foals less than 1 year old. It is caused by a deficiency in selenium and possibly vitamin E and commonly is precipitated by sudden exercise or other stresses. Two clinical syndromes are recognized. The subacute form, which causes generalized myasthenia and dysphagia, is considered herein. In the acute form, myocardial myodegeneration leads to cardiovascular failure and death.

CLINICAL SIGNS RELATING TO WEAKNESS OF THE MUSCLES OF THE NECK, TRUNK, AND LIMBS

The motor unit disorders listed in Table 14.2-1 cause symmetric weakness of muscles of the neck, trunk, and limbs. The resultant tetraparesis ranges in severity from mild ab-

normalities in posture and gait, to recumbency and inability to stand. Weak horses often adopt a characteristic posture, with a base narrow ("elephant on a tub") stance, low head carriage, and with the hindquarters supported against the stable wall. In an attempt to relieve weak postural muscles, weak horses frequently shift weight among all four limbs when standing, a sign that may be misinterpreted as abdominal or foot pain. With the exception of EMND, which affects predominantly postural muscles, most motor unit disorders lead to reluctance to move, a stiff and stilted gait, short stride length, low arc of foot flight, and toe drag. Weak horses may stumble or buckle at the fetlock, have difficulty standing up and lying down, and spend increased periods recumbent. Muscular tremors are a common and often prominent sign of myasthenia. Importantly, tremors and myalgia (muscle pain) are exaggerated by muscular activity and by stressful stimuli and cease when the muscle is rested. Horses with profound myasthenia or myalgia often have generalized sweating, tachycardia, and tachypnea. Horses with myasthenia and/or myalgia may be unable or unwilling to posture to urinate, resulting in bladder distention.

Motor unit dysfunction often causes atrophy of affected muscles, because of varying combinations of neurogenic atrophy, primary muscle pathology, disuse atrophy, and cachexia. Atrophy may be especially marked in horse with EMND and EGS. Although motor unit

dysfunction is characterized by flaccid paralysis, with hyporeflexia and hypotonia, its diagnostic value is limited by the practical difficulties of assessing muscle reflexes and tone in adult horses. Although bulbar, neck, trunk, and anal muscle tone and reflexes are assessed readily in most horses, appendicular muscle tone and reflexes can be assessed only in recumbent horses. Flaccid paralysis is a notable feature only in disorders of the neuromuscular junction. Assessment of muscle tone and reflexes in myopathies is often unrewarding because of swelling and hardening of affected muscles. Resting muscle tone is unremarkable in EMND and EGS. Episodes of HYPP may commence with hypertonia, followed by hypotonia. Motor unit disorders do not cause ataxia or sensory deficits, although the resulting stumbling gait can look like ataxia.

Lifting one forelimb enhances detection of subtle forelimb weakness. It exaggerates muscular tremors and discomfort and ultimately causes buckling and collapse of the weight-bearing limb in markedly weak horses. Pulling on the mane or tail or pushing perpendicularly against the horse may detect weakness of forelimbs, hindlimbs, trunk, and neck. These procedures should be performed when the horse is standing and walking. Horses with motor unit dysfunction are unable to resist the lateral forces applied during these procedures and are readily pulled toward, or pushed away from, the examiner. In contrast, horses with myasthenia resulting from upper motor neuron lesions ("wobblers") can resist lateral forces that are applied while they are standing, because they are able to fix the limb in extension. Care should be taken to avoid exacerbating muscle weakness when performing such procedures.

ANATOMIC DISTRIBUTION OF MUSCLE GROUPS THAT ARE AFFECTED IN MOTOR UNIT DISORDERS

Although all motor unit disorders cause weakness of the muscles of the neck, trunk, and limbs, some disorders also affect other muscles (see Table 14.2-1). The distribution of affected muscles may aid differentiation of these disorders.

Equine motor neuron disease affects predominantly postural muscles, which contain a high component of type I myofibers. Consequently, horses with EMND are unable to lock their passive stay apparatus and appear weaker when standing than when moving. They may have an elevated tailhead because of neurogenic atrophy and subsequent contracture of the sacrocaudalis dorsalis medialis muscles.

Although horses with EGS and EMND adopt similar postures when standing, the pathogenesis of apparent diffuse myasthenia in EGS is unknown. In contrast to horses with EMND, horses with EGS do not have overt myasthenia when assessed by tail and mane pulling, and by lifting a forelimb. Horses with EGS have bilateral ptosis, which is most readily evidenced by downward angulation of the eyelashes. Detection of subtle, bilateral ptosis in EGS and neuromuscular junction disorders is facilitated by instillation of 0.05% phenylephrine eye drops into one conjunctival sac. This reverses the ptosis on the ipsilateral side, probably by direct stimulation of α_1 -adrenoreceptors on the muscles that elevate the eyelid. Although this procedure aids detection of ptosis, it does not indicate the un-

derlying etiology, and false-positive responses occur in sedated horses.

Disorders of neuromuscular junctions cause a more diffuse and potentially more severe muscle weakness than EMND and EGS. Bulbar muscle (i.e., those innervated by cranial nerves) and ocular muscle weakness is often prominent and may be recognized at an earlier stage than limb weakness. This leads to ptosis, mydriasis, reduced pupillary light response, absence of facial expression, and failure to dilate the nostrils after nostril occlusion. Weakness of the tongue, cheeks, muscles of mastication, pharynx, and larynx may cause dysphagia, quidding, drooling of saliva, nasal regurgitation of food and water, soft palate displacement, dysphonia, and aspiration pneumonia. Tongue weakness is readily evident as a reduction in the normally strong retraction that follows gentle withdrawal of the tongue.

Offering the horse food and water can aid detection of weakness of the muscles of prehension, mastication, and deglutition. Inability to swallow food occurs before inability to swallow water. Neuromuscular junction disorders also cause weakness of the orbicularis oculi, anal, retractor penis, and intercostal and diaphragmatic muscles. Tail weakness is detected readily in advanced cases; however, assessment of mild weakness is limited by the substantial variability noted in tail tone among normal horses. Horses with disorders of the neuromuscular junction may die from flaccid paralysis of the respiratory muscles.

Muscular weakness in HYPP may be diffuse or confined to the head. Occasionally, pharyngeal and upper airway muscle weakness causes dysphagia, stridor, and respiratory distress.

Myodegenerative disorders affect predominantly the muscles of the shoulder, hindlimbs, and back, because these contain a high proportion of type II myofibers. However, cardiac and respiratory muscles also may be affected in atypical myoglobinuria, nutritional myodegeneration, and ionophore toxicity. Nutritional myodegeneration also may affect muscles of mastication and muscles of the tongue and pharynx, leading to dysphagia.

ADDITIONAL CLINICAL SIGNS AND SIGNALMENT THAT AID DIFFERENTIAL DIAGNOSIS

Differentiation of motor unit disorders is often possible using only the signalment and clinical findings (Table 14.2-2). Indeed the diagnoses of botulism, postanesthetic myasthenia syndrome, tick paralysis, and EGS usually are based solely on these criteria. A full clinical examination including neurologic examination, orthopedic examination, ophthalmoscopy, and gait evaluation is warranted.

Horses with EMND often show progressive weight loss for 1 month before the onset of muscular weakness, despite having a normal to increased appetite. They may have coprophagia and excessive sweating. Fundic examination reveals a mosaic pattern of dark yellow to dark brown lipofuscin deposits in the tapetum and at the tapetal-nontapetal junction in approximately 30% of cases.

HYPP is the only motor unit disorder characterized by intermittent episodes of muscular weakness. Episodes typ-

Table 14.2-2

Summary of Features that May Aid Differentiation of Motor Unit Disorders

Disorder	Signalment	Additional Clinical Signs	Diagnostic Aids
EMND	Older, single horse affected; often limited access to pasture or fresh green forage	Marked weight loss, despite normal or increased appetite, often precedes onset of muscular weakness; fundic lesions; sweating; horses weaker when standing than moving	Histologic examination of spinal accessory nerve and/or sacro-caudalis dorsalis medialis muscle; muscle enzymes moderately elevated; low plasma vitamin E
Botulism	Ingestion of contaminated food including silage; foals grazing in pastures that harbor spores; rarely toxicoinfection from wound infection; outbreaks possible	Variable autonomic signs, including ileus, constipation, and megaesophagus	Definitive diagnosis rarely achieved; diagnosis supported by detection of toxin in fresh food, serum, and feces, or culture of organism from feces or food; false-positives and false-negatives occur; EMG findings supportive
Postanesthetic myasthenia syndrome	Difficulty or inability to stand after general anesthesia	Same as for botulism; rapid recovery	None
Tick paralysis	Foals infested with ticks	Presence of ticks	None; response to tick removal
Myasthenia gravis	Single horse affected; exercise-induced episodes of recumbency		Detection of autoantibodies to motor endplate; response to glucocorticosteroids
Hyperkalemic periodic paresis	Single horse affected; affects pure and crossbred Quarter Horses, American Paint Horses, and Appaloosas; horses usually well muscled; signs usually recognized <3 years of age	Episodic; most horses are clinically normal between episodes; episodes typically last 15-60 minutes but may extend to several hours; episodes often begin with hypertonia	Definitive diagnosis by DNA testing; usually hyperkalemic during episodes; muscle enzyme levels are normal or elevated; EMG findings supportive
Generalized postanesthetic myopathy	Difficulty or inability to stand after general anesthesia	Stiff, stilted gait; firm, swollen, and painful muscles; distress, sweating, tachycardia, tachypnea, myoglobinuria	Markedly elevated muscle enzymes; myoglobinuria
Severe equine rhabdomyolysis syndrome	After exercise	Same as for generalized postanesthetic myopathy	Markedly elevated muscle enzymes; myoglobinuria
Atypical myoglobinuria	Typically affects horses and ponies grazing in poor-quality pasture, with no supplementary feeding and no exercise; possible outbreaks	Stiff, stilted gait; variable muscle pain, distress, sweating, tachycardia, tachypnea; myoglobinuria; many horses alert, responsive, normal appetite; variable ileus, dysphagia, and urinary retention	Markedly elevated muscle enzymes; myoglobinuria; histopathology of muscle biopsies
Nutritional myodegeneration (subacute skeletal form)	Regions with selenium-deficient soils; mainly foals <1 year old; group outbreaks possible	Stiff, stilted gait; firm, swollen, painful muscles; myoglobinuria; variable distress, sweating, dysphagia, tachycardia, and tachypnea	Markedly elevated muscle enzymes; myoglobinuria, low erythrocyte glutathione peroxidase activity; low blood and tissue selenium and possibly low vitamin E
Acute ionophore toxicity	Ingestion of ionophores such as monensin; out-breaks possible	Acute toxicity causing muscular weakness, hypovolemic shock, and hemolysis; possible generalized sweating, ataxia, myoglobinuria, cardiac dysrhythmias, ileus, colic, diarrhea, dyspnea, and sudden death	Detection of monensin in feed or stomach contents; markedly elevated muscle enzymes; myoglobinuria
Equine grass sickness	Young horses grazing in high-risk areas; seasonal peak in spring; may have multiple cases; recent pasture change	Signs relating to dysfunction of autonomic and enteric neurons, including ileus, colic, ptosis, dysphagia, sweating, tachycardia, and rhinitis sicca	Rhinitis sicca is considered to be pathognomonic; histology of ileal biopsy

ically last 15 to 60 minutes but may extend to several hours before spontaneous resolution. They vary in frequency from single to daily occurrences. Episodes often begin with hypertonia of the facial muscles, causing retraction of the lips and eyelids, prolapse of membrana nictitans, and stiffness of the jaws. This progresses within several minutes to diffuse muscle weakness and tremors. Dog-sitting or recumbency may result. Involvement of muscles of pharynx and larynx may cause stridor. Horses have generalized sweating but are usually alert and non-painful. Rarely, horses die during episodes from cardiac or respiratory failure. Clinical findings and laboratory parameters are usually normal between episodes, although some horses have partial upper airway obstruction during periods of stress or exercise.

Disorders of the neuromuscular junction and EGS may cause smooth muscle weakness because of autonomic dysfunction. Indeed the most striking clinical features of EGS reflect dysfunction of autonomic and enteric neurons, and include ileus, colic, ptosis, dysphagia, rhinitis sicca, sweating, and tachycardia. Rhinitis sicca is considered pathognomonic for EGS. Horses with botulism have variations in the relative severity of smooth muscle, bulbar, and appendicular weakness that may in part reflect differences in the type of botulinum toxin encountered.

Motor unit disorders cause variable degrees of myalgia. Severe myalgia with resultant anxiety, distress, generalized sweating, tachycardia, tachypnea, and expiratory grunting is a prominent feature of postanesthetic myopathy and severe ERS. In contrast, horses with atypical myoglobinuria and nutritional myodegeneration may show only mild myalgia, despite having significant myonecrosis.

Myodegeneration results in myoglobinuria. High concentrations of myoglobin result in dark brown discoloration of the urine, whereas lower concentrations may be detected using the orthotoluidine impregnated test strip present on urine dipsticks. Although this test strip gives a positive response with myoglobin and hemoglobin, the presence of myoglobin presumptively is confirmed by recognition of clinical signs consistent with myodegeneration, and absence of signs of hemolysis including anemia, icterus, and hemoglobinemia.

USE OF ANCILLARY DIAGNOSTIC TESTS TO DIFFERENTIATE MOTOR UNIT DISORDERS

Equine motor neuron disease is confirmed by histologic examination of biopsies of the sacrocaudalis dorsalis medialis muscle and/or spinal accessory nerve. Both techniques have a sensitivity and specificity approximating 90% when assessed by a suitably experienced pathologist. Biopsies from horses with EMND reveal neurogenic atrophy and reinnervation of the muscle, and degeneration of myelinated axons. A low α -tocopherol level supports the diagnosis, although low levels also may occur in apparently healthy horses and in horses with nutritional myodegeneration. Needle electromyography (EMG) reveals spontaneous fibrillation potentials and trains of positive sharp waves. Although this supports a diagnosis of EMND, similar findings may occur in horses with myopathies. To eliminate interference from multiple motor

unit action potentials generated by volitional activity and movement, EMG may be performed in the sacrocaudalis dorsalis medialis muscles under caudal epidural anesthesia. This avoids the requirement for general anesthesia, which carries increased risks in horses with diffuse muscular weakness.

A definitive diagnosis of botulism rarely is achieved. The diagnosis is supported by culture of *Clostridium botulinum* from feed, gastrointestinal contents or tissues, or by detection of botulinum toxin in feed, serum, plasma, or gastrointestinal contents. However, such analyses must be interpreted with caution because bacteria and toxin may be detected in feces from some healthy horses. Toxin rarely is detected in serum or plasma. A diagnosis of botulism is supported by demonstration of brief, small amplitude, overly abundant motor unit action potentials on needle EMG of appropriate muscle, at least in foals.

A diagnosis of acquired myasthenia gravis is supported by detection of antibodies to motor endplates, and by reversal of muscle weakness following treatment with glucocorticosteroids.

HYPP is diagnosed definitively by genetic testing for the HYPP gene. A whole blood sample in EDTA should be submitted to the Veterinary Genetics Laboratory, HYPP Testing, University of California, Davis CA 95616-8744. Although no false-positive horses have been identified, some positive horses may not develop signs, probably because of management factors. The presence of hyperkalemia, hyponatremia, and hemoconcentration during episodes of HYPP supports the diagnosis; however, occasionally episodes occur without hyperkalemia. Genetic testing has superseded potassium chloride challenges and EMG assessment.

A diagnosis of myodegeneration is supported by marked increases in serum activities of creatine kinase (typically >10,000 IU/L), aspartate transaminase (usually >2000 IU/L), and lactate dehydrogenase (LDH; usually >5000 IU/L). In contrast, the other motor unit disorders produce only mild to moderate elevations in the activities of these enzymes. The LDH isoenzyme profile has been used to differentiate myodegeneration of skeletal (predominantly LDH4 and LDH5) and cardiac (predominantly LDH1 and LDH2) muscles; however, this does not always correlate with the distribution of myodegeneration found at necropsy. Although elevated serum troponin levels have been used as an indicator of myocardial damage, this test has not been fully evaluated in horses. Low plasma and tissue selenium levels, low erythrocyte glutathione peroxidase activity, and possibly low serum α -tocopherol levels support a diagnosis of nutritional myodegeneration. However, results of these analyses must be interpreted with caution because some clinically healthy horses have low indices of selenium and vitamin E status. Myodegenerative disorders may be confirmed by histologic examination of biopsies from affected muscles, but this is rarely necessary. EMG demonstrates myopathic potentials in myopathies. Ionophore toxicity can be confirmed by detection of ionophores in feed or stomach contents.

EGS can be diagnosed definitively *pre mortem* only by histologic examination of an ileal biopsy. However, this requires a midline or flank laparotomy, which may be detrimental to case survival.

TREATMENT AND PROGNOSIS

General supportive care is an important consideration when managing horses with diffuse myasthenia. Horses should be stall rested and receive minimal stress. Deep bedding should be provided to minimize decubital ulceration. Massage and physiotherapy may aid muscle function. Dysphagic horses may be given gruels of grass or alfalfa pellets by stomach tube twice daily. Parenteral nutrition is a suitable, but expensive, alternative. Urinary output should be assessed because horses that are weak or recumbent may have urine retention because of an inability to posture to urinate. Bladder distention is confirmed readily by *per rectum* bladder palpation and relieved using an indwelling urinary catheter. Constipation, occurring in horses with autonomic dysfunction such as botulism and EGS, and in horses that are recumbent for any reason, may be managed using mineral oil, fluids, and electrolytes. Recumbent horses may be supported with slings; however, prolonged recumbency and inability to stand often are considered to indicate a hopeless prognosis and prompt euthanasia on humane grounds.

Horses with EMND should receive a readily available form of vitamin E (dl- α -tocopherol, 5 to 7000 IU q24h PO) and increased access to fresh green forage. All horses in the stables should be supplemented because other horses may be affected subclinically. Dimethyl sulfoxide (DMSO; 1 g per kg as 20% solution IV) and corticosteroids may be beneficial in the acute phase. Approximately 40% of EMND horses improve within 6 weeks of treatment, 40% stabilize but remain disfigured, whereas 20% are euthanized because of further deterioration. Athletic function rarely recovers.

Early administration of botulinum antitoxin can increase survival rate in horses with botulism from approximately 10% to 30% without antitoxin to 70% with antitoxin. Crystalline penicillin (20,000-40,000 IU per kg IV q6h) commonly is administered to foals with toxicoinfectious botulism, although this does not eliminate *C. botulinum* from the intestinal tract. Ocular lubricants should be used to prevent corneal ulceration. Mechanical ventilation is indicated in horses with respiratory paralysis. Drugs that potentiate neuromuscular weakness, including aminoglycosides, procaine penicillin, tetracyclines, and magnesium-based laxatives should be avoided. Although neostigmine, guanidine chloride, and 4-aminopyridine may improve muscle function temporarily, they are not recommended because muscle function subsequently may deteriorate because of depletion of acetylcholine. Horses that survive botulism have a complete, but often protracted, recovery.

All three horses with postanesthetic myasthenia syndrome recovered within 7 days with solely supportive care. Foals with tick paralysis usually recover 1 to 3 days after tick removal. Suspected acquired myasthenia gravis cases have responded to titrated doses of prednisolone (1 mg per kg PO q12h) tapering off over weeks to months.

Although mild episodes of HYPP may self-resolve, more severe cases should receive 23% calcium gluconate (0.2-0.4 ml/kg diluted in 2 L of 5% dextrose, slow IV), or 5% dextrose (4.4-6.6 ml/kg IV), or sodium bicarbonate (1-2 mEq/kg IV). A temporary tracheostomy may be required in horses with significant upper airway obstruction. Although affected horses have a lifelong susceptibility to episodic weakness, the frequency and severity of episodes

may be reduced with appropriate control measures. These are described in detail elsewhere (CTEM3, p. 117) but include provision of a low potassium diet, avoidance of sudden dietary changes, frequent feeding, regular exercise, avoidance of glucocorticoids, and administration of acetazolamide (2 to 4 mg per kg PO q12h).

The prognosis for myodegenerative disorders is guarded because many are euthanized for humane reasons because of intractable pain and prolonged inability to stand. General management of these disorders includes administration of analgesics and correction of fluid, electrolyte, and acid-base imbalances. Horses with myoglobinuria should receive large volumes of intravenous and/or oral fluids to induce diuresis and reduce myoglobin-induced renal dysfunction. DMSO may reduce further oxidant mediated muscle damage, whereas dantrolene sodium (2-4 mg per kg IV or 10 mg per kg PO) may reduce excessive calcium release within muscle cells. Acepromazine may aid muscle blood flow. Horses that are recumbent with postanesthetic myopathy should be maintained in sternal recumbency or supported by slings where possible. Intractable horses may be sedated to prevent violent unsuccessful attempts to stand because this may exacerbate muscle injury or lead to orthopedic injury.

Horses with nutritional myodegeneration should receive parenteral selenium (0.06 mg/kg) and vitamin E. This treatment may be repeated at 3 and 10 days after the initial dose. Because combined selenium and vitamin E preparations typically contain insufficient vitamin E, additional vitamin E supplementation is warranted. Foals with mild nutritional myodegeneration may improve rapidly with treatment, but foals that are unable to stand rarely survive.

Treatment of ionophore toxicity is largely supportive. Mineral oil or activated charcoal may reduce further absorption of ionophore. Fluid and electrolyte therapy may help counteract hypovolemia. Intravenous magnesium and phosphate have improved the outcome in experimentally induced toxicity. The prognosis is dependent on the particular compound and the dose ingested. Horses often die in the acute phase, whereas survivors may have long-term complications and rarely regain exercise performance because of myocardial dysfunction.

Currently no specific treatment exists for EGS. As horses with acute or subacute EGS invariably die, they should be euthanized on humane grounds as soon as a diagnosis is made. Some mild chronic cases survive, but recovery takes many months. Supportive care, and the criteria for selection of cases that are suitable candidates for management, are described in detail elsewhere (CTEM4, p. 203).

Supplemental Readings

- Divers TJ, de Lahunta A, Hintz HF et al: Equine motor neuron disease. *Equine Vet Educ* 2001; 13:63-67.
- Lofstedt J: White muscle disease of foals. *Vet Clin North Am Equine Pract* 1997; 13:169-185.
- Naylor JM: Hyperkalemic periodic paralysis. *Vet Clin North Am Equine Pract* 1997; 13:129-144.
- Whitlock RH, Buckley C: Botulism. *Vet Clin North Am Equine Pract* 1997; 13:107-128.

CHAPTER 14.3

Ataxia Associated with Cervical Spinal Cord Disease

JEROME VAN BIERVLIET
Ithaca, New York

A neurologic examination of a patient with suspected cervical spinal cord disease most commonly reveals clinical signs related to deficits in the upper motor neuron system (UMN) and the general proprioception system (GP). The UMN system is responsible for the regulation of muscle tone in support of the body against gravity and the initiation and coordination of voluntary movement. Descending UMN fibers generally are located in the ventral funiculi and the deep portions of the lateral funiculi of the spinal cord white matter. The GP system's function is mainly to detect and transmit the state of position or movement of different muscles, tendons, and joints. Ascending GP fibers are located mostly in the dorsal and superficial dorsolateral funiculi of the spinal cord white matter. Clinical signs seen with cervical spinal cord disease are always a combination of deficits in both systems. Attributing clinical signs to either system individually is almost impossible and not important.

CLINICAL SIGNS OF CERVICAL SPINAL CORD DISEASE

Ataxia (incoordination), spasticity (stiffness) in movement, and paresis (weakness) in all four limbs are the clinical signs caused by a cervical spinal cord lesion. Clinical signs are commonly more obvious in the pelvic than thoracic limbs. Evaluation of postural reactions is almost impossible in adult horses and can be dangerous for the examiner. Therefore the neurologic exam aimed at spinal cord disease consists primarily of judicious evaluation of the gait on a nonslippery floor. Several maneuvers require more complicated coordination and therefore might exacerbate the clinical signs. Head elevation can worsen spasticity in all four limbs and result in floating of the thoracic limbs. Head elevation also sometimes can elicit dragging of the front feet. Some mild floating can be present even in healthy horses.

Walking the horse in tight circles is probably the most sensitive clinical test of UMN/GP deficits. The animal with such deficits is slow in protraction of the limbs, commonly pivots on the inside limb, circumducts the outer limb in a spastic way, sometimes drags the feet, steps on itself, or strikes the inside of its own limbs. Asymmetry may vary given different circle directions. Repeating this maneuver with the head slightly elevated, on a slight slope or more rapidly often can make subtle abnormalities more noticeable.

Paresis can be subjectively evaluated by pulling the horse's tail or mane suddenly to either side (preferably when the horse is in the weight-bearing phase of the gait on the ipsilateral limb). Sometimes the horse stumbles in an attempt to correct its posture. When a spinal cord lesion is present at cervical segments (C1-C6), signs of ataxia and paresis may occur in all four limbs, although the signs are commonly more pronounced in the hind limbs. Spinal cord disease also commonly results in difficulty backing up. The maneuver appears awkward, the limbs can drag and protract slowly. In severe cases the horse can fall backwards. These signs should be differentiated from a loss of balance. This can be especially difficult in horses with a high cervical spinal cord lesion (C1-C2). In those cases, clinical signs can mimic a vestibular problem with a head tilt and tendency to lean to one side. No nystagmus or loss of balance is present, however.

During the neurologic examination, additional signs can be observed that can assist in localizing a lesion. A lesion in the cervical spinal cord between C6-T2 also results in tetraataxia, that is, tetraparesis/tetraplegia, but signs of lower motor neuron deficits (LMN) may be present only in the front limbs. The latter are characterized by weakness, denervation atrophy, and possibly loss of nociception (response to painful stimuli). When the exiting nerve roots are affected in any cervical spinal cord lesion, LMN signs also can be present along certain segments. These signs include denervation atrophy, pain of neurogenic origin, and tremors. Horner's syndrome (sympathetic denervation) also can result from a T1-T3 lesion because the sympathetic innervation of the head exits the spinal cord in this region. Rarely, the syndrome also can occur in the presence of cervical spinal cord disease. The typical clinical signs of Horner's syndrome are unilateral sweating, miosis (constricted pupil), entophthalmia (retraction of the eyeball), and mild ptosis (drooped eyelid).

Laryngeal adduction can be assessed as an indicator of normal neural function. When the horse is slapped with a flat hand in the saddle area, laryngeal adduction occurs on the opposite side. This adduction can be observed by use of an endoscope. The reflex has not completely been mapped. The stimulus is conducted by the ascending spinal nerves, crosses over in the gray matter, ascends in the white matter on the opposite side to the nucleus ambiguus (origin of the vagus nerve) in the brainstem, and then descends in the vagus nerve to the recurrent laryngeal nerve. Cervical spinal cord lesions can result in ip-

ilateral deficit in this test, but damage to the other parts of this reflex must be ruled out.

CERVICAL STENOTIC MYELOPATHY

In cervical stenotic myelopathy (CSM), compression of the cord by two adjacent vertebrae causes signs of cervical spinal cord disease. Two types of CSM can be recognized. The first results from malformation and malarticulation of the vertebrae and is a developmental disease. Therefore it occurs most commonly in younger horses between 6 months and 3 years of age. All breeds are affected, but Thoroughbred horses are predisposed. It is more frequent in males, especially in fast-growing individuals. The second type results from compression of the spinal cord resulting from osteoarthritis of the articular processes, likely superimposed on an abnormally narrow spinal canal. This is seen most commonly in older horses of all breeds.

CSM is most commonly of insidious onset and has a progressive nature. Acute exacerbation after a traumatic episode is common in the history. Mild ataxia may commonly be missed by the owner and may be the cause of the falling episode. The incidence of CSM is strongly correlated with the occurrence of other developmental joint problems, such as osteochondrosis dissecans (OCD) in other joints of the body.

Pathogenesis and Pathology

Multiple pathologic changes can be seen in cases of CSM, and individuals often have several of these bony and soft tissue changes. In the first type, malformation of the vertebra results in a disproportionate vertebral body with apparent caudal extension of the dorsal vertebral arch and a narrower spinal canal, especially at the cranial vertebral orifice (funnel shape). Also this malformation results in instability between the adjacent vertebrae with secondary changes, such as subluxation of the vertebrae, dorsal flare of the caudal epiphysis of the vertebrae, degenerative osteoarthritis of the articular processes. Some soft tissue changes also can be involved in the compression, among them thickening of the ligamentum flavum on the floor of the spinal canal and extradural synovial cysts. The microscopic abnormality seen in the bone and physis of these vertebrae has the characteristics of osteochondrosis.

Several factors have been implicated in the development of CSM. The higher incidence of CSM in certain breeds supports a genetic basis. However, attempts to display the nature of the inheritance have failed and therefore genetic predisposition is most likely only one factor among many. Rapid growth and gender also seem to play a role. Dietary predisposing factors implicated are heavy carbohydrate feeding, copper deficiency, and zinc excess. Environmental factors in the development include trauma and exercise level.

With the first type of CSM, the compression is typically located in the midcervical region and occurs between the caudal end of one vertebral foramen and the cranial vertebral foramen of the next vertebra. Frequently flexion of the neck during cervical myelography makes compression worse, therefore it is called a *dynamic lesion*.

The CSM seen in older horses is primarily due to severe

osteoarthritis of the articular processes. This is associated with extensive bone proliferation compressing the spinal cord dorsolaterally. Still, osteoarthritis of the articular processes is seen commonly in normal older horses. It is therefore likely that some predisposing factors must be present for compression to occur, such as generalized narrowing of the spinal canal. Compression is most common in the caudocervical vertebral joints. During cervical myelography, the compression is often most obvious in the neutral or extended view. Frequently, however, the compression is similar on both the flexed and the neutral view, this is then called a *static compression*.

Clinical Signs

Tetraataxia and tetraparesis (UMN/GP) as described above are the main clinical signs. The clinical signs are symmetric but usually more obvious in the hind limbs. Rarely a noticeable asymmetry is due to asymmetric bony proliferation. No cervical pain is present in most cases, except in older horses with CSM type II. Signs of OCD in joints other than those of the spine also can be suggestive of CSM type I. No clinical signs related to lower motor neuron deficits are present. Cerebrospinal fluid is normal in gross appearance but sometimes can be mildly xanthochromic. Protein level and cell count are within normal limits. CSF analysis is indicated primarily to rule out other differential diagnoses.

Imaging

To confirm suspicion of CSM that is based on the history, signalment, and clinical signs, ancillary diagnostics should include survey radiographs taken with the horse standing in a neutral posture, that is, the head and neck are neither flexed nor extended. Several characteristic observations can be graded, as follows:

1. Mild subluxation of the vertebrae, seen as the degree of dorsal angulation between the adjacent vertebrae
2. Physeal enlargement and dorsal projection of the caudal epiphysis of the vertebral body
3. Osteoarthritis and bony proliferation of the articular processes
4. Osteochondrotic changes, such as incomplete or delayed postnatal ossification at the articular processes.
5. Apparent caudal extension of the vertebral arch over the caudal physis of the vertebral body

Additionally, an objective measurement of the sagittal ratio can help estimating the relative size of the spinal canal. The sagittal ratio is the ratio of the minimum sagittal diameter of the spinal canal to the maximum sagittal diameter of the vertebral body, taken at the cranial aspect of the vertebra and perpendicular to the spinal canal (Figure 14.3-1). This ratio eliminates differences caused by body size and radiographic magnification. A ratio below 52% for C3-C4, C4-C5, C5-C6 and below 56% for C6-C7 is indicative of spinal canal narrowing and indicates that the horse is likely to be affected by CSM. The sensitivity and specificity of the test is approximately 90%. This measurement does not indicate accurately the site of compression, however,

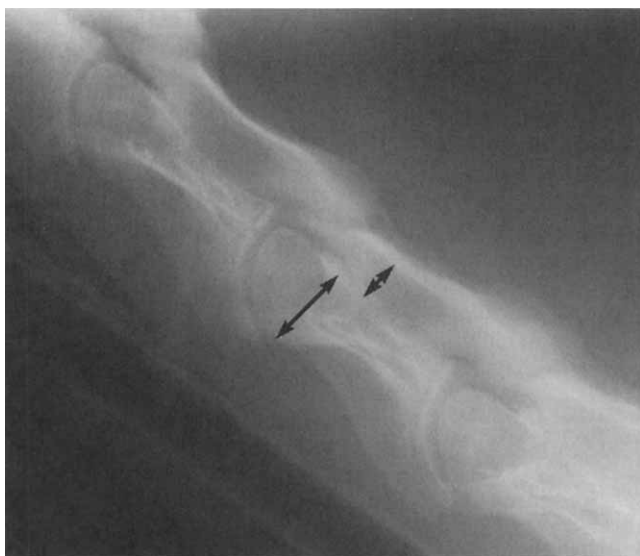


Figure 14.3-1 The sagittal ratio is the ratio of the minimum sagittal diameter of the spinal canal (*small arrows*) over the maximum sagittal diameter of the vertebral body (*large arrows*).

and may not have the same sensitivity and specificity in all case populations.

Cervical myelography traditionally has been considered the gold standard for detection of the site of compression. The horse is placed in lateral recumbency under general anesthesia and a spinal needle is placed in the subarachnoid space of the cisterna magna. The preferred contrast medium in the horse is iohexol (iodine 350 mg/ml), and a volume of 50 to 75 ml is injected slowly into the subarachnoid space. After the injection and the removal of the needle, the horse's head and neck are elevated at approximately 30 degrees for 5 to 10 minutes to aid in the caudal flow of the contrast medium. Three radiographic views are usually necessary for visualization of all cervical vertebrae (craniocervical, midcervical, and caudocervical). These views should be evaluated in neutral, flexed, and extended position. Adequate flexion of the neck has been achieved when the horse's nose touches the carpi. The diagnostic criteria for compression based on myelographic observations have not been established definitively. Reduction of the dorsal myelographic column at the intervertebral junction to 50% or more of that within the vertebra has traditionally been used to predict compression at this site.

Recent studies, however, indicate that this result should be interpreted conservatively, as the diagnostic accuracy of this criterion is less than desirable. It is likely that more compression (up to 70% reduction of the dorsal myelographic column) is necessary to avoid false-positive diagnoses. It seems especially difficult to diagnose the site of compression correctly in CSM cases because affected horses can have a narrow spinal canal at several sites. Flexion of the neck exacerbates the compression of CSM cases especially in the mid cervical region. However, flexion of the neck also may create reduction of the dorsal myelo-

graphic column in normal horses and lead to a false-positive diagnosis. Myelography is fairly safe in the horse, although a proportion of the horses can have complications after recovery. Complications range from seizures and cortical blindness to nonsuppurative meningitis and associated fever. Mostly these complications are self-limiting.

Computed tomography to diagnose CSM is of limited value due to the size limitations (most machines accommodate only the horse's head and neck up to C4), and to the fact that the horse's neck must remain in extension during the procedure.

Treatment

Medical treatment may be successful in growing horses and is aimed at reduction of bony growth, adequate bony maturation with adequate enlargement of the vertebral foramina, and relief of spinal cord compression. Long-term dietary management in growing animals should include restriction of both energy and protein intake (75% of calculated NRC requirements has been suggested) and horses should be supplemented with adequate vitamins and minerals (especially selenium, copper, vitamin E). Stall confinement also is recommended. This regime has been reported to be successful at reducing the incidence of CSM in foals that have been judged to be "highly likely" to develop CSM based upon repeated radiographic examination. After an acute exacerbation of clinical signs resulting from trauma, several antioxidant and antiinflammatory treatments are indicated (DMSO, vitamin E, nonsteroidal antiinflammatory drugs, and glucocorticoids).

Surgery remains the preferred treatment for CSM affected horses. Intervertebral fusion is the surgical technique used for dynamic and static compression. In dynamic compression, fusion of adjacent vertebrae in an extended, noncompressed position avoids further compression. In cases of static compression, the immobilization of the vertebrae aims to create atrophy of previously hypertrophied soft tissue structures and to prevent further bony proliferation. Only one study has evaluated the results of the surgery on the neurologic status. In this study, improvement of clinical signs was noticed in 70% of the surgically treated horses and 46% of the horses were able to achieve athletic performance.

EQUINE DEGENERATIVE MYELOENCEPHALOPATHY

A diffuse degeneration of the spinal cord and some nuclei of the brainstem characterize equine degenerative myeloencephalopathy (EDM). This is a disease that mostly affects younger animals (less than 2 years of age), although some animals may be presented at a later age. It has been reported in different horse breeds in different parts of the world, but the higher incidence in certain breeds (Morgans, Arabians, Appaloosas) and in certain related families indicates the likelihood of a genetic predisposition. Vitamin E deficiency early in life also has been implicated. Clinical signs are insidious in onset and are progressive in nature, although signs may plateau at any stage. Recovery has not been reported.

Pathologic Observations, Pathogenesis, and Clinical Signs

Diffuse axonal degeneration and other changes, such as myelin digestion and astrogliosis, can be seen throughout all sections of the spinal cord. White and gray matter are affected. Several proprioceptive relay nuclei in the brainstem and spinal cord also are affected.

Because of the diffuse nature of the pathology, the clinical signs are symmetric and commonly as severe in the front as in the hind limbs. The gait is spastic and stiff. Marked hyporeflexia over the neck and trunk is also reported, including absent slap-test, cutaneous trunci reflex, cervicofacial reflex. No other clinical signs are noticed.

Several factors probably are involved in the development of EDM. Genetic predisposition seems likely due to the familial occurrence. Vitamin E deficits early in life during a critical stage in growth have been implicated in the pathogenesis because supplementation of vitamin E has reduced the incidence of EDM in problem herds. At the time that clinical signs become apparent, the serum vitamin E level can be normal. Other suspected etiologic factors, such as chronic exposure to organophosphates, are still unproven.

Cerebrospinal fluid is normal on gross appearance and microscopic evaluation. It is difficult to differentiate this disease from other differential diagnosis (especially CSM). Therefore other diseases must be ruled out and the definitive diagnosis of EDM can be made only by histopathologic evaluation of the spinal cord.

Treatment and Prognosis

Treatment should include vitamin E supplementation (2000 to 3000 IU/day) orally and continuously. Ample green forage of good quality is also a good source for vitamin E. Prognosis, however, is poor because remission or recovery from EDM has not been reported. Treatment therefore is aimed at stabilizing the clinical signs. Because of possible inheritance of this disease, breeding of affected animals and their parents should be discouraged.

SPINAL CORD TRAUMA

Spinal cord trauma in the horse typically occurs after a fall or other traumatic incident. This may or may not be accompanied by vertebral fractures. The cervical vertebrae are a common site for vertebral fractures, especially the atlas and axis in foals. The lower cervical and cranial thoracic sites are more common fracture sites in adult horses. Rarely does a fracture occur in horses secondary to other pathology, such as vertebral osteomyelitis or neoplasia.

Presenting clinical signs depend on the location and severity of spinal cord trauma. Ataxia can vary from mild deficits to complete recumbency. In recumbent animals the practitioner may find it difficult to assess the neurologic status of the patient accurately because of the body size. With cervical lesions between the C1 and C6 segment, the animal has normal or increased spinal reflexes in thoracic and pelvic limbs. Only animals with severe damage to their spinal cord lose perception of noxious stimuli in the limbs. Animals with high cervical lesions

may not be able to turn their heads sideways. Vertebral fractures are usually painful and crepitus often can be elicited with manipulation of the neck. Some horses with vertebral fractures exhibit only pain and stiffness without neurologic signs.

Diagnosis and Imaging

Survey radiographs should be taken in the trauma patient. Vertebral fractures usually can be detected, but sometimes it requires ventrodorsal or oblique views to demonstrate the fracture. Contrast myelography can help to detect a site of compression, such as a subdural hematoma or fracture site. Computed tomography is superior for small or complicated fractures, especially in foals in which numerous growth plates can confuse the radiographic interpretation. CSF analysis commonly reveals signs of hemorrhage, either acute (high protein, red blood cell count) or long-standing (xanthochromia, high protein).

Treatment and Prognosis

If vertebral fractures compress the spinal cord or if the risk of displacement of fragments is great, surgery may be required to relieve compression and stabilize the fracture fragments. In some cases, a fiberglass cast with the neck in extension is adequate to prevent displacement and compression. Callus formation after healing of a fracture site can compress the spinal cord several months after the initial trauma.

Medical treatment for spinal cord trauma should be aimed at antiinflammatory and antioxidant therapy. Corticosteroids and nonsteroidal antiinflammatory drugs are aimed at decreasing the inflammation. In acute cases, mannitol (0.25 to 1 mg/kg as a 20% solution IV over 20 minutes) can help to decrease vasogenic edema and tissue swelling. Oxidative damage is important in the pathogenesis of CNS trauma and therefore treatment with antioxidants can be warranted (vitamin E, vitamin C, DMSO, mannitol).

Prognosis is difficult to assess in most cases and depends on the severity of the neurologic deficit, the nature of possible fractures, and the duration of spinal cord compression. Because of the slow healing of the nervous tissue, it can be months before the final definitive outcome is known.

OTHER CAUSES OF CERVICAL CORD DISEASE

Equine Protozoal Myeloencephalitis

Equine protozoal myeloencephalitis (EPM; see Chapter 2.11: "Equine Protozoal Myeloencephalitis") can manifest itself in focal, multifocal, or diffuse way, inherent to the occurrence of the parasitic infection. In cases of multifocal or diffuse involvement of the spinal cord, tetra-ataxia and tetraparesis are the predominant clinical signs. Clinical signs commonly are asymmetric. On careful examination differences left to right can be distinguished. Also, lower motor neuron signs or cranial nerve deficits additional to the UMN/GP signs support a diagnosis of EPM.

Equine Herpesvirus-1 Infection

Equine herpesvirus-1 (EHV-1) is a common respiratory pathogen that can induce neurologic signs related to the spinal cord. This disease is discussed in more detail in Chapter 2.2: "Equine Herpesvirus."

Subdural hematomas associated with trauma also can cause clinical signs of cervical spinal cord disease. Neoplasia and epidural abscesses are rare in the horse, especially in the neck.

Supplemental Readings

- Blythe LL, Craig AM: Equine degenerative myeloencephalopathy. Part I. Clinical signs and pathogenesis. *Comp Cont Educ Pract Vet* 1992; 14(9):1215-1221.
- Blythe LL, Craig AM: Equine degenerative myeloencephalopathy. Part II. Diagnosis and treatment. *Comp Cont Educ Pract Vet* 1992; 14(12):1633-1637.
- De Lahunta A: *Veterinary Neuroanatomy and Clinical Neurology*, 2nd edition, pp 219-237, Philadelphia, WB Saunders, 1983.
- Mayhew IG: Tetraparesis, paraparesis and ataxia of the limbs, and episodic weakness. In Mayhew IG (ed): *Large Animal Neurology: A Handbook for Veterinary Clinicians*, pp 243-333, Philadelphia, Lea & Febiger, 1989.

- Mayhew IG, Donawick WJ, Green SL et al: Diagnosis and prediction of cervical vertebral malformation in Thoroughbred foals based on semi-quantitative radiographic indicators. *Equine Vet J* 1993; 25:435-440.
- Moore BR, Reed SM, Biller DS et al: Assessment of vertebral canal diameter and bony malformations of the cervical part of the spine in horses with cervical stenotic myelopathy. *Am J Vet Res* 1994; 55:5-13.
- Moore BR, Reed SM, Robertson JT: Surgical treatment of cervical stenotic myelopathy in horses: 73 cases (1983-1992). *J Am Vet Med Assoc* 1993; 203:108-112.
- Olby N: Current concepts in the management of acute spinal cord injury. *J Vet Intern Med* 1999; 13:399-407.
- Smith MO: Nervous system trauma in horses. *Proceedings of the 19th American College of Veterinary Internal Medicine Forum*, pp 275-277, 2001.
- Van Biervliet J, Scrivani PV, Divers TJ et al: Evaluation of diagnostic criteria for spinal cord compression during cervical myelography in horses. *Proceedings of the 20th American College of Veterinary Internal Medicine Forum*, p 769, 2002.
- Wagner PC, Grant BD, Gallina A et al: Ataxia and paresis in horses. Part III. Surgical treatment of cervical spinal cord compression. *Comp Cont Educ Pract Vet* 1981; 3:S192-S202.

CHAPTER 14.4

Spinal Cord Diseases Causing Paresis and Atrophy in the Limbs

THOMAS J. DIVERS
Ithaca, New York

The lower motor neuron (LMN) system includes both the somatic efferent and visceral efferent parts of the nervous system. Spinal cord disease in the horse that affects the ventral gray matter may cause dysfunction of the somatic efferent system, which is responsible for innervating striated voluntary skeletal muscles. The efferent system also may be damaged near the spinal cord as the axons course through the white matter and exit the cord as the ventral spinal roots ("rootlet" disease). Abnormalities in the efferent system may cause lower motor neuron signs, including muscle weakness, hypotonia, hyporeflexia, and fasciculation of the muscles innervated by the affected nerve or nerves, in addition to neurogenic atrophy of the muscle within as few as 7 days after the onset of disease. Limb reflexes cannot be evaluated in the standing horse but evaluation should be attempted in recumbent horses

and in foals. The reflexes are listed in Table 14.4-1.

Prolonged recumbency and/or myopathy can diminish the diagnostic value of reflex examination. Sensory innervation to different areas of the limb is discussed under peripheral nerve disorders (see Chapter 14.1: "Limb Weakness, Atrophy, and Other Signs of Peripheral Nerve Disease"). Lower motor neuron signs may result from injury to ventral horn cells or rootlets at any location within the cord but are clinically most noticeable at the cervical thoracic and lumbosacral intumescences; the location of the motor neurons that innervate the muscles of the limbs, tail, and anus. Spinal cord diseases that may cause LMN disease to the limbs are listed in Table 14.4-2. Except for equine motor neuron disease (EMND) and dysautonomia (grass sickness), most of these diseases cause signs of both LMN and upper motor neuron (UMN) disease.

Equine Herpesvirus-1 Infection

Equine herpesvirus-1 (EHV-1) is a common respiratory pathogen that can induce neurologic signs related to the spinal cord. This disease is discussed in more detail in Chapter 2.2: "Equine Herpesvirus."

Subdural hematomas associated with trauma also can cause clinical signs of cervical spinal cord disease. Neoplasia and epidural abscesses are rare in the horse, especially in the neck.

Supplemental Readings

- Blythe LL, Craig AM: Equine degenerative myeloencephalopathy. Part I. Clinical signs and pathogenesis. *Comp Cont Educ Pract Vet* 1992; 14(9):1215-1221.
- Blythe LL, Craig AM: Equine degenerative myeloencephalopathy. Part II. Diagnosis and treatment. *Comp Cont Educ Pract Vet* 1992; 14(12):1633-1637.
- De Lahunta A: *Veterinary Neuroanatomy and Clinical Neurology*, 2nd edition, pp 219-237, Philadelphia, WB Saunders, 1983.
- Mayhew IG: Tetraparesis, paraparesis and ataxia of the limbs, and episodic weakness. In Mayhew IG (ed): *Large Animal Neurology: A Handbook for Veterinary Clinicians*, pp 243-333, Philadelphia, Lea & Febiger, 1989.

- Mayhew IG, Donawick WJ, Green SL et al: Diagnosis and prediction of cervical vertebral malformation in Thoroughbred foals based on semi-quantitative radiographic indicators. *Equine Vet J* 1993; 25:435-440.
- Moore BR, Reed SM, Biller DS et al: Assessment of vertebral canal diameter and bony malformations of the cervical part of the spine in horses with cervical stenotic myelopathy. *Am J Vet Res* 1994; 55:5-13.
- Moore BR, Reed SM, Robertson JT: Surgical treatment of cervical stenotic myelopathy in horses: 73 cases (1983-1992). *J Am Vet Med Assoc* 1993; 203:108-112.
- Olby N: Current concepts in the management of acute spinal cord injury. *J Vet Intern Med* 1999; 13:399-407.
- Smith MO: Nervous system trauma in horses. *Proceedings of the 19th American College of Veterinary Internal Medicine Forum*, pp 275-277, 2001.
- Van Biervliet J, Scrivani PV, Divers TJ et al: Evaluation of diagnostic criteria for spinal cord compression during cervical myelography in horses. *Proceedings of the 20th American College of Veterinary Internal Medicine Forum*, p 769, 2002.
- Wagner PC, Grant BD, Gallina A et al: Ataxia and paresis in horses. Part III. Surgical treatment of cervical spinal cord compression. *Comp Cont Educ Pract Vet* 1981; 3:S192-S202.

CHAPTER 14.4

Spinal Cord Diseases Causing Paresis and Atrophy in the Limbs

THOMAS J. DIVERS
Ithaca, New York

The lower motor neuron (LMN) system includes both the somatic efferent and visceral efferent parts of the nervous system. Spinal cord disease in the horse that affects the ventral gray matter may cause dysfunction of the somatic efferent system, which is responsible for innervating striated voluntary skeletal muscles. The efferent system also may be damaged near the spinal cord as the axons course through the white matter and exit the cord as the ventral spinal roots ("rootlet" disease). Abnormalities in the efferent system may cause lower motor neuron signs, including muscle weakness, hypotonia, hyporeflexia, and fasciculation of the muscles innervated by the affected nerve or nerves, in addition to neurogenic atrophy of the muscle within as few as 7 days after the onset of disease. Limb reflexes cannot be evaluated in the standing horse but evaluation should be attempted in recumbent horses

and in foals. The reflexes are listed in Table 14.4-1.

Prolonged recumbency and/or myopathy can diminish the diagnostic value of reflex examination. Sensory innervation to different areas of the limb is discussed under peripheral nerve disorders (see Chapter 14.1: "Limb Weakness, Atrophy, and Other Signs of Peripheral Nerve Disease"). Lower motor neuron signs may result from injury to ventral horn cells or rootlets at any location within the cord but are clinically most noticeable at the cervical thoracic and lumbosacral intumescences; the location of the motor neurons that innervate the muscles of the limbs, tail, and anus. Spinal cord diseases that may cause LMN disease to the limbs are listed in Table 14.4-2. Except for equine motor neuron disease (EMND) and dysautonomia (grass sickness), most of these diseases cause signs of both LMN and upper motor neuron (UMN) disease.

Table 14.4-1
Spinal Reflex Testing

Body Part	Test	Anatomic Location Being Tested
Thoracic limb*	Flexor reflex: pinch skin on distal limb Triceps reflex Cutaneous trunci reflex	Peripheral nerves, muscles of limb, C6-T2 spinal segments Radial nerve, muscles, C7-T1 spinal segments Peripheral nerve, ascending white matter, C8-T1 spinal segments, lateral thoracic nerve, cutaneous trunci muscle
Pelvic limb*	Flexor reflex Patella reflex	Sciatic nerve, muscle, L5-S3 spinal segments Femoral nerve, muscles, L4-L5 spinal segments
Tail and anus	Perineal sensitivity, anal and tail reflex	Pudendal nerve, coccygeal nerves, muscles, S1-S3 spinal segments

C, Cervical; T, thoracic; L, lumbar; S, sacral.

*The muscular tone in each limb should be determined through manipulation of each limb. A flaccid limb with little or no movement is supportive of a lower motor neuron (LMN) disease.

Table 14.4-2
Causes of Lower Motor Neuron Disease

CERVICAL/THORACIC LESIONS		
Frequently Asymmetric Signs	Frequently Symmetric Signs	
Equine protozoal myelitis <i>Sarcocystis neurona</i> <i>Neospora hughesi</i> *	Equine motor neuron disease	
Trauma to cord and/or nerve roots	Equine dysautonomia Grass sickness†	
Nerve root/cord neoplasm Polyneuritis‡		
LUMBOSACRAL LESIONS		
Frequently Asymmetric Signs	Variable Symmetry	Frequently Symmetric Signs
Equine protozoal myelitis <i>Sarcocystis neurona</i> <i>Neospora hughesi</i> *	EHV-1 myelitis	Equine motor neuron disease
	Melanoma§	Equine dysautonomia (grass sickness)†
	Sarcoma Polyneuritis§ Trauma Abscess	

EHV, equine herpesvirus.

*May have more nerve root disease than *S. neurona*.

†Predominantly a lower motor neuron disease of the autonomic nervous system.

‡Rarely affects the front legs.

§Commonly affects tail and anus.

CLINICAL SIGNS

Disease of the ventral gray matter or ventral roots in the cervical-thoracic (C-T) area causes LMN signs in one or both front legs. Proprioceptive deficits of the corresponding front leg(s) and ipsilateral hind limb are observed if the white matter (UMN system) is diseased. Absence of the cutaneous trunci reflex also may be observed. Abnormal

sensation of a part of the front limb and signs of Horner's syndrome might be present if the dorsal or intermediate gray area or dorsal nerve root are diseased. Evidence of pain on manipulation of the lower cervical-upper thoracic area would not be expected unless the corresponding vertebrae or nerve roots are involved.

Diseases of the ventral gray matter or nerve roots in the

lumbosacral (L-S) area cause LMN signs in one or both hindlimbs. Proprioceptive deficits in the same limb may be seen if the white matter is affected. If the sacral gray matter and/or nerve roots (including cauda equina; see Chapter 14.6: "Bladder, Rectal, Anal, and Tail Paralysis; Perineal Hypalgesia; and Other Signs of Cauda Equina Syndrome") are disrupted, LMN signs may be present in the tail, anus, bladder, and hind legs. If the cauda equina is diseased sufficiently, sensory deficits occur to the tail, perineum, and penis but no deficit occurs to the prepuce. Sacral gray matter/nerve root disease may cause "LMN" bladder dysfunction: an atonic, distended bladder that can be expressed easily and urine "dribbling" as the horse walks. This is not a common finding in horses with LMN disease except in cases of polyneuritis equi. Urinary incontinence can be due to UMN disease associated with a severe cord lesion at T1-L6. This frequently is due to EHV-1 myelitis (see Chapter 2.2: "Equine Herpesviruses") and more rarely to equine protozoal myelitis (EPM; see Chapter 2.11: "Equine Protozoal Myeloencephalitis"). The clinical findings with "UMN" bladder dysfunction include distended bladder that is difficult to express because of normal or increased urethral tone and no voluntary urination.

Ventral and intermediate gray matter disease at any location in the cord may cause regional muscle atrophy and occasionally ipsilateral sweating caudal to the lesion.

DIAGNOSIS

The differential diagnoses should be considered after careful clinical examination to determine the following: (1) the neuroanatomic site or sites of the lesion or lesions within the cord, (2) whether the disease is purely LMN or a combination of LMN and UMN, (3) evidence of analgesia or pain in the area, and (4) the speed of progression of clinical signs. The signalment such as age of the horse (most lower motor neuron diseases occur in adults), color of the horse, or historical information such as trauma, abortions, or respiratory disease or previous EPM on the farm or in the region can be important diagnostic information. Equine motor neuron disease, EPM, dysautonomia, and EHV-1 myelitis often have an acute onset of clinical signs, whereas polyneuritis equi and compression of the spinal cord by melanoma generally have an insidious onset with slow progression.

If the presence of LMN signs is unclear, an EMG or muscle biopsy can be helpful. EMG evaluation requires specialized equipment and sometimes considerable experience in interpretation. The muscle biopsy is generally easily and safely performed and is best interpreted by a pathologist experienced in examining equine muscle.

A spinal tap can be helpful in diagnosing EPM, EHV-1, polyneuritis, and trauma. Approximately 15% of the cases of EPM with LMN signs have abnormal CSF cytology (pleocytosis). The CSF often is positive or strongly positive for EPM on Western blot analysis, although a weak positive does not rule out EPM. A positive Western blot suggests the horse has been infected with *Sarcocystis neurona* but does not confirm that EPM is the cause of the LMN signs. Spinal fluid from EHV-1 myeloencephalitis cases routinely has slight yellow discoloration (xanthochromia), elevated protein (>70 mg/dl) and absence of pleocytosis.

Horses with polyneuritis equi frequently have elevated protein with mononuclear pleocytosis in the CSF collected from the lumbosacral area. Fluid may be difficult to collect in some polyneuritis equi cases if the dura mater is thickened. Fluid collected from horses with polyneuritis equi may have elevated antibodies to P-2 myelin protein but sensitivity and specificity of this test have not been well demonstrated. Trauma-induced UMN/LMN disease may be accompanied by normal to variably abnormal CSF depending upon the severity and duration of the injury. There may be gross (red or yellow) discoloration in the presence of acute or subacute trauma. Pleocytosis may develop secondary to the trauma. Radiographs of the cervical-thoracic area may help to confirm a fracture. Radiographs, CAT scan, and even ultrasound examination of the lumbosacral area in foals may reveal a fracture and/or abscess compressing nerve roots.

A rectal examination should be performed in horses with LMN signs at the tail and anus to help to rule out fractures and tumors, especially melanomas in grey horses. Horses with EMND have characteristic signs of LMN disease in all limbs and frequently the neck without any signs of UMN disease. Muscle enzymes often are increased moderately in the acute/subacute stage of EMND, which is unique compared with the findings in other diseases causing LMN (see Table 14.4-2). Vitamin E levels are less than 1 g/ml, and brown pigment (lipofuscin) is visible on ophthalmoscopic exam in approximately 50% of cases of EMND. A muscle biopsy of the dorsosacralis coccygealis muscle (which is often abnormally elevated as a result of neurogenic atrophy and subsequent muscle contracture) or a biopsy of the spinal accessory nerve aids in the diagnosis of EMND.

TREATMENT

Antiprotozoal therapy with ponazuril orally 5 mg/kg or more for at least 28 days is warranted for treatment of EPM. Dimethyl sulfoxide (DMSO) and flunixin meglumine generally are recommended during the first few days of treatment. Immune modulator therapy (levamisole 2 mg/kg PO q24h for 4 days then q48h for 2 weeks) may have some therapeutic merit, as may daily vitamin E.

Horses suffering from EHV-1 myeloencephalitis should be treated with flunixin meglumine and DMSO in mild to moderate cases. More severe and/or rapidly progressing cases should receive dexamethasone (0.05-0.2 mg/kg q24h IV) for 3 to 4 days followed by a tapering dose. Pentoxifylline (7.5 mg/kg PO or IV q 8-12h) and aspirin 90 to 120 grains/adult horse q48h orally may have some beneficial effect in decreasing inflammation and thrombosis. Acyclovir (10 to 20 mg/kg q12h) may be warranted because a few clinically affected horses are still viremic. Antibiotics should be given to protect against bacterial invasion of the respiratory tract or urinary tract infection after catheterization. If the bladder is distended, which it frequently is, urinary catheterization either intermittently or with an indwelling catheter should be performed to prevent chronic stretching of the detrusor muscle. Bethanechol (0.04 mg/kg IV, SQ or IM q8h) and phenoxylbenzamine (0.2-0.4 mg/kg PO q8h) can be used in hopes of improving detrusor activity and relaxing the urethral sphincter.

Fractures and/or infections are best managed by surgical correction/drainage, appropriate antimicrobials based upon culture and sensitivity, and use of antiinflammatory and antioxidant drugs such as mannitol, vitamin E, or DMSO. Vitamin E is the recommended treatment for EMND. Corticosteroids may provide some mild improvement in polyneuritis equi cases but long-term prognosis is poor. Corticosteroids also may be helpful in the rare case of fibrocartilaginous emboli. Autogenous vaccine (Veterinary Oncology Services and Research Center, West Chester, Pa.) has been used for treatment of melanoma, but proof of efficacy is lacking.

A sling should be used for horses that cannot rise to prevent some complications associated with prolonged recumbency, although if the disease is that severe, prognosis for complete recovery is poor. With any LMN disease, appropriate physical therapy and nursing/nutrition care are indicated.

PROGNOSIS

With appropriate therapy, the prognosis for EHV-1 myelitis is good if the horse does not become recumbent. Bladder dysfunction may persist in some cases. The prog-

nosis for EPM cases with LMN signs is highly variable depending upon the duration and severity of clinical signs. Even after apparent recovery, relapses occur in approximately 10% of cases. Horses with nerve root compression by fractures of the spine or a spinal/vertebral abscess have a fair prognosis with appropriate treatment, especially in foals. Approximately 50% of horses with EMND have noticeable improvement after change in nutrition and/or vitamin E supplementation, although full recovery is not possible.

Supplemental Readings

DeLahunta A: Veterinary Neuroanatomy and Clinical Neurology, 2nd edition, pp 53-94, Philadelphia, WB Saunders 1983.

Divers TJ, Mohammed HO, Cummings JF et al: Equine motor neuron disease: findings in 28 horses and proposal of a pathophysiological mechanism for the disease. *Equine Vet J* 1994; 26(5):409-415.

Van Maanen C, Sloet van Oldruitenborgh-Oosterbaan MM, Damen EA et al: Neurological disease associated with EHV-1 infection in a riding school: clinical and virological characteristics. *Equine Vet J* 2001; 33(2):191-196.

CHAPTER 14.5

Thoracolumbar Spinal Cord Disorders Causing Upper Motor Neuron Signs in the Hindlimbs

GILLIAN A. PERKINS

THOMAS J. DIVERS

Ithaca, New York

Spinal cord disease located between T2-L4 spinal cord segments may cause upper motor neuron (UMN) signs in the rear limbs, along with lower motor neuron (LMN) signs (atrophy) of the back muscles if the grey matter in this area is involved. Severe transecting edema and/or infarction deep to the dorsal grey column of the cord in the thoracolumbar region may cause dysuria because of injury to the UMN that supplies the bladder. With UMN bladder dysfunction, little or no voluntary micturition will be present—only reflex micturition.

ETIOLOGY AND CLINICAL SIGNS

The most common diseases affecting the T2-L4 area of the spinal cord in the horse are equine herpesvirus-1 (EHV-1), myeloencephalitis (see Chapter 2.2: "Equine Herpesvirus"),

and equine protozoal myelitis (EPM; see Chapter 2.11: "Equine Protozoal Myeloencephalitis"). EPM can affect any area of the cord, is often asymmetric, and frequently affects white and grey matter in the spinal cord. Loss of lumbar musculature due to lower motor neuron disease is not unusual with EPM that involves the T2-L4 area of the cord. In some cases this loss can be dramatic and often asymmetric. EPM only rarely causes dysuria in the horse. If the lesions are limited to the T2-L4 area, ataxia of the rear limbs can be classified as a grade 1 to 5, with absence of LMN signs (i.e., atrophy, fasciculations, and hyporeflexia) in the rear limbs. Front limb movement is normal. EPM limited to the T2-L4 area generally causes subacute to chronic clinical signs.

For unknown reasons, EHV-1 myeloencephalitis appears to have a predilection for causing lesions in the

Fractures and/or infections are best managed by surgical correction/drainage, appropriate antimicrobials based upon culture and sensitivity, and use of antiinflammatory and antioxidant drugs such as mannitol, vitamin E, or DMSO. Vitamin E is the recommended treatment for EMND. Corticosteroids may provide some mild improvement in polyneuritis equi cases but long-term prognosis is poor. Corticosteroids also may be helpful in the rare case of fibrocartilaginous emboli. Autogenous vaccine (Veterinary Oncology Services and Research Center, West Chester, Pa.) has been used for treatment of melanoma, but proof of efficacy is lacking.

A sling should be used for horses that cannot rise to prevent some complications associated with prolonged recumbency, although if the disease is that severe, prognosis for complete recovery is poor. With any LMN disease, appropriate physical therapy and nursing/nutrition care are indicated.

PROGNOSIS

With appropriate therapy, the prognosis for EHV-1 myelitis is good if the horse does not become recumbent. Bladder dysfunction may persist in some cases. The prog-

nosis for EPM cases with LMN signs is highly variable depending upon the duration and severity of clinical signs. Even after apparent recovery, relapses occur in approximately 10% of cases. Horses with nerve root compression by fractures of the spine or a spinal/vertebral abscess have a fair prognosis with appropriate treatment, especially in foals. Approximately 50% of horses with EMND have noticeable improvement after change in nutrition and/or vitamin E supplementation, although full recovery is not possible.

Supplemental Readings

DeLahunta A: Veterinary Neuroanatomy and Clinical Neurology, 2nd edition, pp 53-94, Philadelphia, WB Saunders 1983.

Divers TJ, Mohammed HO, Cummings JF et al: Equine motor neuron disease: findings in 28 horses and proposal of a pathophysiological mechanism for the disease. *Equine Vet J* 1994; 26(5):409-415.

Van Maanen C, Sloet van Oldruitenborgh-Oosterbaan MM, Damen EA et al: Neurological disease associated with EHV-1 infection in a riding school: clinical and virological characteristics. *Equine Vet J* 2001; 33(2):191-196.

CHAPTER 14.5

Thoracolumbar Spinal Cord Disorders Causing Upper Motor Neuron Signs in the Hindlimbs

GILLIAN A. PERKINS

THOMAS J. DIVERS

Ithaca, New York

Spinal cord disease located between T2-L4 spinal cord segments may cause upper motor neuron (UMN) signs in the rear limbs, along with lower motor neuron (LMN) signs (atrophy) of the back muscles if the grey matter in this area is involved. Severe transecting edema and/or infarction deep to the dorsal grey column of the cord in the thoracolumbar region may cause dysuria because of injury to the UMN that supplies the bladder. With UMN bladder dysfunction, little or no voluntary micturition will be present—only reflex micturition.

ETIOLOGY AND CLINICAL SIGNS

The most common diseases affecting the T2-L4 area of the spinal cord in the horse are equine herpesvirus-1 (EHV-1), myeloencephalitis (see Chapter 2.2: "Equine Herpesvirus"),

and equine protozoal myelitis (EPM; see Chapter 2.11: "Equine Protozoal Myeloencephalitis"). EPM can affect any area of the cord, is often asymmetric, and frequently affects white and grey matter in the spinal cord. Loss of lumbar musculature due to lower motor neuron disease is not unusual with EPM that involves the T2-L4 area of the cord. In some cases this loss can be dramatic and often asymmetric. EPM only rarely causes dysuria in the horse. If the lesions are limited to the T2-L4 area, ataxia of the rear limbs can be classified as a grade 1 to 5, with absence of LMN signs (i.e., atrophy, fasciculations, and hyporeflexia) in the rear limbs. Front limb movement is normal. EPM limited to the T2-L4 area generally causes subacute to chronic clinical signs.

For unknown reasons, EHV-1 myeloencephalitis appears to have a predilection for causing lesions in the

thoracolumbar area. Clinical signs are usually peracute and cause ataxia and paresis of the rear legs that is generally more symmetric than asymmetric. The ataxia/paresis may be mild or severe, causing recumbency with a “dog-sitting” appearance in some horses. The disease progresses mostly in the first 5 days after clinical signs become apparent. Signs of bladder dysfunction are frequently apparent and presumably are due to the severe and radiating edema and/or infarction of the white and grey matter within the T2-L4 area. In less than 25% of cases clinical signs reflect lesions elsewhere in the central nervous system (CNS). The second most common disease site is probably the L4-S3 area, in which LMN signs to the rear limbs, bladder, tail, and anus become apparent.

Other diseases affecting *only* the T2-L4 spinal cord in the horse are not common but include equine degenerative myelopathy (EDM), bony compressive lesions such as sarcoma and fractures, and inflammatory disorders (viral, fungal, or bacterial meningitis). EDM is most common in weanlings, yearlings, and/or young adults and has a hereditary and nutritional basis. An absence of green forage plays a causative role in the disease. Vertebral body abscess in this area is not an uncommon finding in growing foals, especially if a problem with *Rhodococcus equi* is present on the farm. Other differential diagnoses would include nerve root disorders—inflammatory or compressive—within the T2-L4 region. These alone would not cause proprioceptive deficits in the limbs but may cause noticeable atrophy of the muscles of the back.

DIAGNOSIS

The diagnosis of EHV-1 myeloencephalitis is often easy due to the following characteristic findings:

- History of recent respiratory disease or abortion on the premises
- Fever in some neurologically affected horses and in other horses in the stable
- Multiple horses acutely affected with neurologic signs (most often ataxic horses with weakness in the rear limbs)
- Dysuria in a number of the horses with spinal cord signs
- Rapid progression of the disease in some horses

Although highly variable, horses with EHV-1 myeloencephalitis may have more generalized signs of vasculitis, such as limb edema and uveitis. In addition, mules may be on the premises in some outbreaks and can appear to be a risk factor. A laboratory finding of xanthochromia of the cerebrospinal fluid (CSF) without pleocytosis can help diagnose EHV-1 myeloencephalitis. In a few cases herpesvirus may be isolated from blood or nasal culture. Horses that die from the disease should have histopathology and immunocytochemistry performed on the cord to confirm endothelial presence of EHV-1, vasculitis, edema, and infarction radiating through the white and grey matter.

The diagnosis of EPM is based on the ruling out of

other diseases, the horse's response to treatment, and the following factors:

- The disease is most common in young adult performance horses in locations with a previous history of the disease.
- Ataxia of the legs is asymmetric or sometimes symmetric.
- Lumbar muscle wasting develops rapidly in some cases, and evidence of multifocal disease is present in many affected horses.
- Laboratory findings include CSF antibodies specific for *Sarcocystis neurona* that frequently give a moderate to strong Western blot reading and nonsuppurative pleocytosis in a small percentage of cases.

TREATMENT

The treatment of mild to moderate cases of EHV-1 myelitis should include flunixin meglumine and dimethyl sulfoxide (DMSO). More severe and/or rapidly progressing cases should be treated with dexamethasone (0.05-0.2 mg/kg IV q12-24h) to decrease the severity of the CNS vasculitis. Acyclovir (10 mg/kg PO) may be given ideally—both as a treatment because some horses with CNS signs are viremic and as a prophylaxis because the disease is highly contagious. If dysuria is a clinical sign, the bladder should be catheterized to prevent chronic stretching of the detrusor muscle. Either intermittent catheterization or an indwelling catheter can be used. Bethanechol (0.04 mg/kg IV, SQ, or IM q8h) and phenoxybenzamine (0.2-0.4 mg/kg PO q8h) can be used to improve bladder function. Bactericidal antibiotics should be administered to help protect against secondary bacterial infections of the respiratory and urinary tracts. If fecal incontinence is a problem, laxative diets and manual evacuation of the rectum may be required.

Treatment of EPM includes antiprotozoal therapy with ponazuril administered by mouth at a dosage of 5 mg/kg or more for at least 28 days. Flunixin meglumine and DMSO should be used during the early treatment period. Immune modulator therapy, such as levamisole (2 mg/kg PO q24h for 4 days, followed by q48h for 2 weeks), may be beneficial. Vitamin E (2000-6000 IU/horse q24h) is frequently recommended for many CNS disorders, including EPM, but its efficacy is unproven. Physical therapy and excellent nursing care, including slinging if necessary, are important aspects of therapy for any CNS disorder.

PROGNOSIS AND PREVENTION

Horses with EHV-1 myeloencephalitis that do not become recumbent generally have a good prognosis for return to function. A small percentage of horses have permanent deficits in gait and/or bladder functions. Horses that become recumbent rarely return to normal function. Vaccination of all horses for EHV-1 is recommended, although no proof exists that vaccination protects against the neuroendolithrophic strain of the virus.

Horses with EPM have a very variable prognosis that often depends on the duration and/or severity of the dis-

ease. Those horses with chronic and/or relapsing signs generally have a guarded prognosis for return to full athletic function. Horses with an obvious response to treatment within 2 to 4 weeks generally have a good prognosis—although approximately 10% of these cases may relapse with identical clinical signs months later, even after an apparent full clinical recovery.

Prevention of EPM is based on a decrease in the horses' exposure to opossum feces. Whenever possible, all hay and grain should be properly stored to prevent its access to opossums, the definitive host, or to birds or insects that could be possible mechanical vectors. If this type of management is not possible and/or successful, intermittent

treatment may be used—although its efficacy is unproven. A vaccine for EPM is commercially available; its safety has been confirmed, but its efficacy remains unproven.

Supplemental Readings

Dubey JP, Lindsay DS, Saville WJ et al: A review of *Sarcocystis neurona* and equine protozoal myeloencephalitis (EPM). *Vet Parasitol* 2001; 95:89-131.

Friday PA, Scarratt WK, Elvinger F et al: Ataxia and paresis with equine herpesvirus type 1 infection in a herd of riding school horses. *J Vet Intern Med* 2000; 1:197-201.

CHAPTER 14.6

Bladder, Rectal, Anal, and Tail Paralysis; Perineal Hypalgesia; and Other Signs of Cauda Equina Syndrome

R. SCOTT PIRIE
Edinburgh, Scotland

The cauda equina is so named because of its gross resemblance to a horse's tail. It is the tapered caudal end of the spinal cord (conus medullaris) and the caudal extensions of the spinal nerve roots that extend within the vertebral canal, adjacent to and beyond the terminal spinal cord. Because of the disparate rates of longitudinal growth of the spinal cord and vertebral column, these nerve roots extend caudally within the subarachnoid space before they emerge through the meninges. Following their emergence, they continue to course caudally towards their respective intervertebral foramina, where the dorsal and ventral nerve roots fuse to form the spinal nerve. Thus the spinal nerve emerges from the *vertebral column* at a more caudal *vertebral* location than the spinal cord segmental origin of the nerve. For example, in a fully grown horse, the first three sacral spinal cord segments (S1-S3) lie within the last (L6) lumbar vertebra, and the last two sacral (S4-S5) and first several coccygeal spinal cord segments lie within the first sacral vertebra. Additionally, as the meninges terminate at the level of the junction of the second (S2) and third (S3) sacral vertebrae, the more caudal nerve roots extend for a greater distance within the vertebral canal following their emergence through the meninges.

Before consideration of clinical signs resulting from damage to the cauda equina, a precise neuroanatomic definition of the structure is essential. For the purpose of this section, the cauda equina is defined as the nerve roots and terminal spinal cord that are located caudal to an imaginary line drawn between the third and fourth sacral spinal cord segments. This imaginary line would pass approximately through the level of the lumbosacral *vertebral* articulation. It is important to remember that the nerve roots of the first three sacral spinal cord segments extend caudally, almost parallel with the spinal cord, before they emerge through the intervertebral foramina at a level caudal to the aforementioned imaginary line. Therefore the clinical signs that result from damage to the cauda equina can be attributed to damage to any or all of the sacrococcygeal nerve roots, which give rise to the pudendal, caudal rectal, pelvic, and coccygeal peripheral nerves and part of the sciatic and gluteal peripheral nerves.

The term *cauda equina syndrome*, as the name suggests, refers to a single or multiple clinical signs that result from damage to the structures of the cauda equina. The recognition of such clinical signs helps to give an indication of the anatomic location of the lesion or lesions; however, neural damage at the level of the cauda equina may result

ease. Those horses with chronic and/or relapsing signs generally have a guarded prognosis for return to full athletic function. Horses with an obvious response to treatment within 2 to 4 weeks generally have a good prognosis—although approximately 10% of these cases may relapse with identical clinical signs months later, even after an apparent full clinical recovery.

Prevention of EPM is based on a decrease in the horses' exposure to opossum feces. Whenever possible, all hay and grain should be properly stored to prevent its access to opossums, the definitive host, or to birds or insects that could be possible mechanical vectors. If this type of management is not possible and/or successful, intermittent

treatment may be used—although its efficacy is unproven. A vaccine for EPM is commercially available; its safety has been confirmed, but its efficacy remains unproven.

Supplemental Readings

Dubey JP, Lindsay DS, Saville WJ et al: A review of *Sarcocystis neurona* and equine protozoal myeloencephalitis (EPM). *Vet Parasitol* 2001; 95:89-131.

Friday PA, Scarratt WK, Elvinger F et al: Ataxia and paresis with equine herpesvirus type 1 infection in a herd of riding school horses. *J Vet Intern Med* 2000; 1:197-201.

CHAPTER 14.6

Bladder, Rectal, Anal, and Tail Paralysis; Perineal Hypalgesia; and Other Signs of Cauda Equina Syndrome

R. SCOTT PIRIE
Edinburgh, Scotland

The cauda equina is so named because of its gross resemblance to a horse's tail. It is the tapered caudal end of the spinal cord (conus medullaris) and the caudal extensions of the spinal nerve roots that extend within the vertebral canal, adjacent to and beyond the terminal spinal cord. Because of the disparate rates of longitudinal growth of the spinal cord and vertebral column, these nerve roots extend caudally within the subarachnoid space before they emerge through the meninges. Following their emergence, they continue to course caudally towards their respective intervertebral foramina, where the dorsal and ventral nerve roots fuse to form the spinal nerve. Thus the spinal nerve emerges from the *vertebral column* at a more caudal *vertebral* location than the spinal cord segmental origin of the nerve. For example, in a fully grown horse, the first three sacral spinal cord segments (S1-S3) lie within the last (L6) lumbar vertebra, and the last two sacral (S4-S5) and first several coccygeal spinal cord segments lie within the first sacral vertebra. Additionally, as the meninges terminate at the level of the junction of the second (S2) and third (S3) sacral vertebrae, the more caudal nerve roots extend for a greater distance within the vertebral canal following their emergence through the meninges.

Before consideration of clinical signs resulting from damage to the cauda equina, a precise neuroanatomic definition of the structure is essential. For the purpose of this section, the cauda equina is defined as the nerve roots and terminal spinal cord that are located caudal to an imaginary line drawn between the third and fourth sacral spinal cord segments. This imaginary line would pass approximately through the level of the lumbosacral *vertebral* articulation. It is important to remember that the nerve roots of the first three sacral spinal cord segments extend caudally, almost parallel with the spinal cord, before they emerge through the intervertebral foramina at a level caudal to the aforementioned imaginary line. Therefore the clinical signs that result from damage to the cauda equina can be attributed to damage to any or all of the sacrococcygeal nerve roots, which give rise to the pudendal, caudal rectal, pelvic, and coccygeal peripheral nerves and part of the sciatic and gluteal peripheral nerves.

The term *cauda equina syndrome*, as the name suggests, refers to a single or multiple clinical signs that result from damage to the structures of the cauda equina. The recognition of such clinical signs helps to give an indication of the anatomic location of the lesion or lesions; however, neural damage at the level of the cauda equina may result

from various causes. If multiple neurologic deficits are detected and if each can be explained by damage at this site, focal damage to the structures of the cauda equina is likely. However, it should be highlighted that such neurologic deficits may occur in isolation, whereby consideration should be given to nerve damage outside the vertebral canal—namely, at any point along the motor unit from the emergence of the spinal nerve from the intervertebral foramen to the neuromuscular junction. Also, certain diseases may result in multifocal lesions, which clinically manifest consistently with damage to the cauda equina but also induce neurologic deficits elsewhere.

CLINICAL SIGNS

The most common clinical signs that arise from damage to the cauda equina include tail paralysis or weakness, anal hypotonia or atonia, rectal and bladder paralysis or weakness, and relaxation and protrusion of the penis. Other clinical signs include lack or absence of skin sensation (hypalgesia or analgesia) of the tail, anus, and skin of the perineum and muscle atrophy of the coccygeal muscles. Occasionally hind limb weakness, ataxia and muscle atrophy has been associated with damage at the more cranial aspect of the cauda equina region. The number and severity of clinical signs observed depends largely on the location and severity of the neural damage, which in turn depends largely on the underlying cause.

Tail paralysis or weakness can be appreciated by a lack of tail tone and lack of resistance to manipulation. Excessive urine soaking in mares and fecal contamination of the underside of the tail may reflect an inability to elevate the tail during defecation and urination, respectively. Additionally, the reflex clamping down of the tail that follows a touch stimulus of the anus may be absent. If tail paralysis is present in the absence of other neurologic deficits, specific damage to the coccygeal spinal cord segments, coccygeal nerve roots, or coccygeal nerves is likely. An example of such injury is nerve root avulsion as a result of excessive traction to the tail. It is important to consider that other neurologic deficits that result from damage at the level of the cauda equina may prevent obvious recognition of tail paralysis. For example, when rectal paralysis is also present, defecation may not be possible, and fecal staining of the tail may not be observed.

Anal hypotonia or atonia may be appreciated by the presence of a dilated anus and by an absent or sluggish anal reflex. Although paralysis of the anal sphincter may result in fecal incontinence, rectal paralysis is almost invariably also present if the site of damage is within the cauda equina because both the sensory (pudendal and caudal rectal nerves) and motor (pelvic nerves) innervation to both the anus and rectum originate from the same spinal cord segments (S2-S4). Therefore a reduced frequency of defecation is a more common clinical sign with damage at this site because of the accumulation of excessive quantities of fecal material within the rectum. Bladder paralysis results in urinary incontinence with urine dribbling, thus resulting in vaginal hyperemia and scalding of the perineum and medial thighs in mares and scalding of the dorsal aspect of the hind limbs, medial thighs, and ventral abdomen in males.

As the urinary incontinence seen with cauda equina damage results from lower motor neuron damage to the parasympathetic supply to the detrusor muscle (pelvic nerves), the bladder is atonic and distended and can be expressed manually during transrectal examination. This appearance contrasts with upper motor neuron damage, whereby conscious urine voiding may be lost. However, detrusor muscle contraction can be activated when the bladder is filled beyond a certain threshold volume. Under these circumstances, the bladder may feel moderately enlarged during transrectal palpation; however, it is not easily expressed manually during this procedure. Consequently, transrectal palpation of the urinary bladder in cases with upper motor neuron damage may not reveal any obvious differences from cases with no neurologic deficits at all.

Relaxation and protrusion of the penis may result from damage to the motor unit anywhere from the spinal cord segments S2-S4, via the spinal nerve roots, the spinal nerves, and the pudendal nerve to the neuromuscular junction on the retractor penis muscle. However, in relation to cauda equina syndrome, the spinal cord segments and/or spinal nerve roots of S2-S4 are the sites of damage, and consequently other neurologic deficits consistent with damage at this site will be present.

Although not clinically obvious, a detailed neurologic examination may reveal insensitivity to painful stimulation of the skin around the anus and perineum, which extends up to 20 cm lateral to the anus and ventrally. Sensory innervation to the skin in these areas is supplied by the pudendal and caudal rectal nerves, which originate in the spinal segments S2-S4. Therefore if loss of sensation in these areas has resulted from damage to the cauda equina, other neurologic deficits detailed above are also likely to be present. Occasionally, an area of increased cutaneous responsiveness to nonpainful and painful stimuli may be located encircling the area of hypalgesia or analgesia—sometimes resulting in self-mutilation by means of tail and perineal rubbing.

DISEASES THAT COMMONLY MANIFEST WITH THESE CLINICAL SIGNS

Diseases that commonly manifest with a combination of the above clinical signs include traumatic damage to the cauda equina, neuritis of the cauda equina, equine herpesvirus-1 (EHV-1) myeloencephalitis, and Sorghum-Sudan grass toxicity.

Traumatic Damage to the Cauda Equina

Trauma is the most common cause of cauda equina syndrome. Traumatic events—such as falling over backwards, breeding injuries, backing into walls, or overlying obstructions such as a closed top stable door or a horizontal side bar of stocks—may result in a variety of injuries to the sacrum, including fractures and luxations. The location and severity of the injury will determine the extent of damage to the cauda equina and consequently the severity and nature of the neurologic deficits exhibited. Although such trauma will usually result in immediate clinical signs, signs may be delayed, or additional signs may

appear after an interval of time because of continued neural damage following the initial trauma. This delayed or subsequent neural damage may result from instability of fractures or from the formation of hematomas, calluses, abscesses, or scar tissue. Damage to the more cranial aspect of the cauda equina—at the level of the first and second sacral vertebrae—may result in damage to all sacrococcygeal spinal segments and/or nerve roots. This may be manifest clinically by multiple neurologic deficits, including pelvic limb signs due to damage to some of the nerve roots making up the gluteal and sciatic nerves. By contrast, damage to the caudal aspect of the cauda equina at the level of the fifth sacral or any of the coccygeal vertebrae may result in limited neurologic deficits restricted to tail paralysis and hypalgesia/analgesia. As previously mentioned, such restricted damage to the nerve roots of the coccygeal spinal cord segments may occur after excessive traction on the tail. Damage immediately caudal to the second sacral vertebrae will likely result in many of the clinical signs described previously, such as bladder, anal, and rectal paralysis; perineal hypalgesia; and tail signs in the absence of pelvic limb signs.

Neuritis of the Cauda Equina

Neuritis of the cauda equina is a condition that has been repeatedly described in the European and North American literature and is considered as a disease of the adult horse. The disease reflects neuritis of the nerve roots of the cauda equina and results from a granulomatous reaction at this site, although several cases of accompanying cranial nerve deficits have been described and most commonly involve the facial, trigeminal, and vestibulocochlear nerves. The deficits attributable to damage at the cauda equina are often yet not always symmetrical, whereas cranial nerve deficits are frequently asymmetric and have been noted to improve on one side and appear on the opposite side. The involvement of these other nerve roots has led to the disease also being termed *polyneuritis equi*.

Although the precise etiology of cauda equina neuritis is unknown, evidence exists to support the involvement of an autoimmune response against the myelin of especially the cranial and sacrococcygeal extradural nerve roots, with previous viral and bacterial infections having been implicated in the initiation of this response. The neurologic deficits primarily reflect lower motor neuron paralysis at the level of the cauda equina and are usually progressive yet may attain a certain level of severity, following which they become static. Although not always present, the coexistence of cranial nerve deficits will help to distinguish this disease from other conditions that result in damage to structures of the cauda equina, such as sacral trauma. However this author is aware of cases of trauma that have resulted in multifocal lesions, thus causing both cranial nerve (facial and vestibulocochlear) and cauda equina signs.

Equine Herpesvirus-1 Myeloencephalitis

The reader should refer to Chapter 2.2 for a more detailed discussion of EHV-1 infection. The neurologic form of EHV-1 infection has a worldwide distribution. Although

outbreaks of the neurologic form have been extensively reported, it is considerably less common than the abortigenic and respiratory forms of EHV-1 infection. Equine EHV-1 myeloencephalitis is thought to result from central nervous system infarction caused by vasculitis, which is initiated in the endothelial cells of small blood vessels. The clinical signs are abrupt in onset and usually nonprogressive after approximately 24 hours. Many horses spontaneously recover—either completely or partially. The most obvious neurologic deficits result from spinal cord damage, and although signs such as anal hypotonia and urinary incontinence of the lower motor neuron type consistent with damage to the cauda equina are often present, limb ataxia and paresis are much more clinically evident. The limb deficits are usually symmetrical, and although the thoracic limbs are usually much less involved than are the pelvic limbs, their involvement helps distinguish this EHV-1 myeloencephalitis from other conditions that result in signs attributable to involvement of the cauda equina.

Sorghum-Sudan Grass Toxicity

Ingestion of plants of the *Sorghum* species, such as Sorghum or Sudan grass may result in neurologic deficits consistent with some involvement of the cauda equina. The underlying mechanism probably reflects toxic damage to the central nervous system. Although the precise toxin is unknown, cyanogenic glycosides and lathyrogen-like substances have been implicated as possible causal factors. Because the clinical signs are related to the feeding of *Sorghum* species, outbreaks have occurred in groups of horses, and evidence exists to suggest that the cyanide content of *Sorghum* plants is increased during rapid growth, drought, and freezing. Although many of the clinical signs reflect involvement of the cauda equina—such as perineal muscle relaxation, protrusion of the penis, tail paresis, and urinary incontinence caused by overflow from a distended, atonic bladder—most cases will initially present with pelvic limb ataxia and paresis. Occasionally, a characteristic “bunny hopping” gait will be seen, wherein both hindlimbs are lifted off the ground simultaneously.

Equine Protozoal Myeloencephalitis

The reader should refer to Chapter 2.11 for a more detailed discussion of equine protozoal myeloencephalitis (EPM). Horses with EPM exhibit a wide array of clinical signs, and neuronal damage by the parasite *Sarcocystis neurona* may result in signs consistent with cauda equina involvement. As with many cases of EPM, clinical signs are often asymmetric and attributable to very selective neuronal damage.

Sacrococcygeal Vertebral Osteomyelitis

Osteomyelitis of the sacral or coccygeal vertebrae may result in paravertebral abscess formation and secondary inflammation and/or compression of the nerve roots of the cauda equina, thus resulting in the lower motor neuron signs described previously. Most common in the newborn, vertebral osteomyelitis is usually caused by hematogenous

spread from a distant infection or septicemia. *Rhodococcus equi* may be particularly prone to causing this condition in foals.

Rabies

Loss of tail and anal sphincter tone are among the variety of clinical signs reported in cases infected with the neurotropic rabies virus; however, these signs usually occur late in the disease process. As the classic signs of rabies do not occur reliably enough to permit the disease to be reasonably ruled out in most suspect cases, consideration must be given to the possibility of this diagnosis in any horse that exhibits obscure and indistinct neurologic signs. This is especially the case if the horse is showing obvious signs of either depression or—less commonly—mania.

Neoplasia

Neoplasia can be considered an extremely rare cause of clinical signs associated with involvement of the cauda equina. Extradural neoplasms such as lymphosarcomas, melanomas, and neurofibromas may result in compression of the cauda equina, with subsequent development of typical neurologic deficits.

Caudal Meningitis

Rarely, inflammation of the cauda equina may occur secondarily to bacterial caudal meningitis. *Cryptococcus neoformans* has been implicated in this condition and, interestingly, a single report exists in the literature of cauda equina syndrome and vestibular disease and facial nerve paralysis in a pony—the result of suppurative myelomeningitis from which *Listeria monocytogenes* was isolated.

Verminous Myelitis

This author is unaware of any report of cauda equina syndrome that results from aberrant helminth migration; however, consideration may be given to this possibility because both *Strongylus vulgaris* larvae and *Setaria* species have both been reported to result in spinal cord disease in donkeys and horses, respectively.

DIAGNOSTIC STRATEGY

Careful consideration of the signalment may be useful in ruling out possible diagnoses when one is faced with a case that exhibits neurologic deficits consistent with damage to the cauda equina. For example, extradural neoplasms, although rare, will usually occur in older animals. Additionally, although cauda equina neuritis has been confirmed in a yearling filly, this is rare; it is generally considered a disease of the adult horse. Consideration of certain aspects of the history may be extremely helpful. A history of sacral trauma that preceded the development of neurologic deficits consistent with damage to the cauda equina would certainly warrant careful attempts to detect a sacral fracture or subluxation. A recent history of respiratory disease and/or abortion within a year may accompany the development of cauda equina signs associated with EHV-1 in-

fection. Obviously if the condition affects a number of horses that graze *Sorghum* species, plant toxicity should be considered from the beginning of the investigation.

Despite the obvious benefits gained from consideration of the signalment and history, a careful and detailed physical and neurologic examination will likely help considerably in differentiating between the possible causes of damage to the cauda equina. For example, both external and transrectal palpation of the sacrum may be useful in detecting an obvious displaced fracture or subluxation. Although detection of abrasions and injuries elsewhere may be consistent with a fall with possible sacral trauma, it is important to consider the possibility that such a fall may have occurred as a result of previously existing ataxia, and may not necessarily be the cause of the neurologic deficits. The purpose of a detailed neurologic examination is to detect and assess the severity and symmetry of any neurologic deficits and to establish whether such deficits can be attributed entirely to damage at the level of the cauda equina. If additional neurologic deficits are present and cannot be attributed to cauda equina damage, consideration must be given to the probable existence of diffuse and/or multifocal disease. For example, although it is not consistent, the involvement of cranial nerve signs in some cases of cauda equina neuritis will help to differentiate it from conditions such as sacral trauma and EHV-1 myeloencephalitis; however, consideration should be given to multiple trauma-induced lesions. The presence of severe hind limb ataxia and weakness and/or the presence of thoracic limb signs is more indicative of involvement of spinal cord segments more cranial to the cauda equina and is more consistent with diffuse or multifocal neural damage as seen in, for example, EHV-1 myeloencephalitis, *Sorghum* species toxicity, EPM, and rabies.

Additionally, certain ancillary diagnostic tests may prove beneficial in confirming or ruling out certain diagnoses. The detection of sacral fractures may be aided by the use of radiography, nuclear scintigraphy, and ultrasonography. Complete blood counts are of little value in differentiating between the different causes of cauda equina syndrome. Although a neutrophilic leukocytosis may reflect an inflammatory process associated with bacterial meningitis and epidural abscessation, many chronic cases of bladder paralysis may have a similar inflammatory profile secondary to the infectious process that occurs within a paralyzed urinary bladder. Similarly, urinalysis findings are often consistent with those expected in cases of cystitis. Serology may be of some benefit in supporting some of the possible diagnoses. The detection of serum anti-P2 (myelin protein of peripheral nerves) antibodies with an ELISA test strongly supports a diagnosis of neuritis of the cauda equina. In suspected cases of EHV-1 myeloencephalitis, the assessment of paired serum samples for anti-EHV-1 antibodies is indicated. Although a fourfold increase in virus neutralizing antibody titer is reported to highly support the diagnosis, evaluation of acute and convalescent serum samples may not always be diagnostic, particularly in young horses that may not develop high titers after their first exposure. Additionally, high or rising complement fixation (CF) antibodies 2 to 3 weeks after the onset of signs are also reported to indicate recent EHV-1 infection, and this test is thought to be more sensitive than virus neu-

tralization for detecting rising titers. Other tests that may strongly support a diagnosis of EHV-1 myeloencephalitis include the identification of EHV-1 in or isolation of EHV-1 from the respiratory tract or buffy coat.

Analysis of cerebrospinal fluid (CSF) from the lumbosacral site may be useful in many cases of cauda equina syndrome. Horses with neuritis of the cauda equina may have moderately increased protein levels in the CSF (>80–150 mg/dl) as well as elevated white blood cell counts that is usually due to increased lymphocyte counts. As the lesions in cauda equina neuritis are predominantly extradural, this diagnosis may also be supported by the detection of chronic inflammatory changes at this level by cytologic analysis of fluid obtained from epidural lavage with a 20 ml aliquot of sterile saline. Although horses with EPM may also have moderately elevated protein levels and cell counts, the diseases may be differentiated by testing CSF for both anti-*Sarcocystis neurona* antibody by immunoblot test and the presence of *S. neurona* by the nested polymerase chain reaction. CSF analysis in cases of EHV-1 myeloencephalitis often reveals xanthochromia and an albuminocytologic dissociation often with marked elevations in CSF protein concentrations (up to 480 mg/dl) and normal nucleated cell counts, although such changes may be absent if CSF is collected very early in the disease process. The fact that some horses develop an elevation in CSF albumin/serum albumin ratios suggests that the elevated protein levels result from albumin leakage into CSF as a result of vascular endothelial damage. Evaluation of CSF antibody concentrations is not regarded as a dependable diagnostic test for EHV-1 infection, although identification of EHV-1 in or isolation of EHV-1 from the CSF supports this diagnosis.

In cases of sacrococcygeal trauma, CSF may be normal to bloody in appearance, usually without an elevated nucleated cell count. Vertebral damage caudal to S2 is less likely to result in CSF changes, as the meninges terminate at this level; however, cytologic examination of an epidural lavage may be diagnostically beneficial. As epidural abscesses are located outside the meninges, CSF changes are unlikely to be helpful in such cases and perhaps only mildly reflect an adjacent inflammatory process; however, parasitic migration and meningitis will often result in a dramatic elevation in the CSF granulocyte count. CSF analysis from rabies cases often yields normal results, particularly at the onset of disease, although some cases may show a mild pleocytosis, with a predominance of macrophages and lymphocytes. However, consideration should be given to the benefits of such analyses when weighed against the risks, which include potential exposure to low levels of the virus in CSF.

Finally, histopathologic examination of coccygeal nerve root biopsies—obtained by use of blind needle biopsy or arthroscope—may be useful in the diagnosis of cauda equina neuritis.

TREATMENT

In many cases, specific treatment of the underlying cause of the neurologic lesion that results in cauda equina syndrome is not available. However, supportive nursing care is extremely important in all cases, regardless of the un-

derlying cause. As voluntary urination is compromised or absent, bladder drainage is necessary either by frequent (twice daily) catheterization or the insertion of an indwelling catheter. Additionally, the oral administration of antibiotics such as trimethoprim-sulfadiazine is recommended to treat or reduce the risk of cystitis. As many cases of bladder paralysis of the lower motor neuron type will rapidly accumulate large quantities of sabulous sediment within the bladder, repeated lavage, and siphoning cycles may be required to reduce the severity of this secondary complication. It is believed that the accumulation of large quantities of sabulous sediment in the bladder may in itself result in myogenic bladder dysfunction. Therefore failure to remove this sediment, in cases in which the underlying neurologic problem resolves, may result in continuation of urinary incontinence. Urinary acidifiers, such as oral ammonium chloride powder, have been advocated to reduce sediment formation; however, their use has been met with limited success. In addition, their poor palatability may preclude their use in many cases. In cases of urinary incontinence, the frequent application of petroleum jelly to the perineum and hind limbs will help to prevent urine scalding.

Frequent evacuation of feces from the terminal rectum is often necessary to prevent impaction colic. The provision of diets that promote soft feces, such as a complete pelleted diet or bran supplements, may be helpful in preventing rectal impactions, as will the intermittent administration of mineral oil. Consideration may be given to the use of a parasympathomimetic drug such as bethanechol (0.25–0.75 mg/kg SQ or PO q12h or q8h) to stimulate bladder and rectal emptying; however, this drug has yielded limited success. Horses with cauda equina syndrome secondary to sacrococcygeal trauma are usually treated medically for the first 1 to 2 weeks with antiinflammatory therapy, including dimethyl sulfoxide, corticosteroids and nonsteroidal antiinflammatory drugs. If no improvement is seen within 2 months, permanent neurologic dysfunction is likely. Depending on the type of sacrococcygeal vertebral damage, certain surgical procedures have been described to aid resolution. These include cauda equina decompression by dorsal laminectomy or hemilaminectomy of the caudal part of the sacrum in adults and reduction and stabilization of fractures in foals. Additionally, surgical drainage of epidural abscesses and removal of diseased bone from cases of sacral osteomyelitis is indicated in specific cases.

No specific therapy has been shown to be effective in cases of cauda equina neuritis, but treatment with corticosteroids at antiinflammatory doses early in the course of the disease has been suggested to be helpful. However, because of the severity of the clinical signs, the gradual deterioration, the poor prognosis, and the development of secondary complications in animals maintained on supportive care, euthanasia is usually the eventual choice. Complete resolution of cauda equina syndrome is likely in horses that survive EHV-1 myeloencephalitis and possible in horses treated appropriately for EPM. No specific treatment exists for cases of *Sorghum* toxicity; however, withdrawal of *Sorghum* plants from the diet results in a gradual improvement in clinical signs over weeks to months, although recovery may not be complete. Larvicidal doses of anthelmintics are indicated in suspected cases

of verminous myelitis, but no specific treatment is available for cauda equina cases caused by neoplasia or rabies.

Supplemental Readings

Chaffin MK, Honnas CM, Crabill MR et al: Cauda-equina syndrome, diskospondylitis, and a paravertebral abscess caused by *Rhodococcus equi* in a foal. *J Am Vet Med Assoc* 1995; 206:215-220.
 Collatos C, Allen D, Chambers J et al: Surgical-treatment of sacral fracture in a horse. *J Am Vet Med Assoc* 1991; 198:877-879.

Mayhew IG: Urinary bladder distension, dilated anus, and atonic tail: the cauda equina syndrome. In Mayhew IG: *Large Animal Neurology: A Handbook for Veterinary Clinicians*, pp 349-357, Philadelphia, 1989, Lea & Febiger.

Scarratt WK, Buechner-Maxwell VA, Karzenski S et al: Urinary incontinence and incoordination in three horses associated with equine protozoal myeloencephalitis. *J Equine Vet Sci* 1999; 19:642-645.

Yvorchuk-St. Jean K: Neuritis of the cauda equina. *Vet Clin North Am Equine Pract* 1987; 3(2):421-428.

CHAPTER 14.7

Idiopathic and Rare Neurologic Diseases

CONSTANZE FINTL
 Edinburgh, Scotland

STRINGHALT

Stringhalt is a disease of unknown etiology that has been recognized in horses for centuries. It is characterized by an abnormal gait with involuntary and exaggerated flexion of the hock and stifle of one or both hindlimbs during attempted movement. Stringhalt is typically a disease of individual animals; however, outbreaks have been recorded and are often called Australian stringhalt although outbreaks have also been recorded in New Zealand and North and South America. The classic or sporadic form usually only involves one limb, whereas during outbreaks it often involves both hindlimbs—although one may be more severely affected and even the thoracic limbs can be affected. In its milder form it will usually not limit the performance of the horse, but in the more severe cases it can be a debilitating disease.

Clinical Syndrome

This condition is easily recognizable by the characteristic gait; however, the severity and hence the degree and duration of hyperflexion varies. The severity is often graded from 1 to 5; a grade 1 affected horse displays only mildly exaggerated flexion during backing and turning, and this may disappear during exercise. At the other end of the spectrum, in a grade 5 horse, the fetlock may hit the ventral surface of the abdomen or the point of the elbow during attempted movement. In the case of bilateral stringhalt, forward movement is difficult—especially in the more severely affected cases—and the horse will likely display a plunging, bunny-hopping gait. Involvement of the thoracic limbs is seen as hyperextension and very stiff

movements of the limbs. Rarely, recumbency may result in severely affected horses.

The reason for the characteristic and exaggerated hock flexion is poorly understood, but some have suggested that damage to the reflex arc controlling muscle tone (gamma efferent reflex arc) at one or several points disrupts normal postural tone and coordination of muscle contraction. When damage involves motor fibers to skeletal muscles, it eventually leads to muscle fiber denervation and atrophy.

It is likely that a lesion could exist at any point of the reflex arc or of its connections—that is, it could involve the stretch receptors in the muscle fiber, the afferent nerve, the central nervous system (CNS) synapse, upper motor neuron connections, gamma efferent fibers and muscle spindles, and finally alpha motor axons, the neuromuscular junction, and the muscle itself. In other words, stringhalt may be a consequence of a sensory or motor neuropathy, spinal cord disease, or myopathy.

The cause of either form of this disease has not yet been determined, although previous trauma may be involved in individual cases, whereas a fungal or plant toxicity is suspected where outbreaks occur. Injury to the hock appears to sometimes cause this syndrome—presumably through damage to control of the muscle spindle trigger mechanism. Sometimes after injury, months may elapse before signs of stringhalt develop.

Several studies have tried to identify the pathology of Australian stringhalt outbreaks. This has revealed primary damage to axons in the long peripheral nerves that supply the pelvic limbs. Presumably, small diameter nerve fibers are affected before large diameter motor fibers, thus ac-

of verminous myelitis, but no specific treatment is available for cauda equina cases caused by neoplasia or rabies.

Supplemental Readings

Chaffin MK, Honnas CM, Crabill MR et al: Cauda-equina syndrome, diskospondylitis, and a paravertebral abscess caused by *Rhodococcus equi* in a foal. *J Am Vet Med Assoc* 1995; 206:215-220.
Collatos C, Allen D, Chambers J et al: Surgical-treatment of sacral fracture in a horse. *J Am Vet Med Assoc* 1991; 198:877-879.

Mayhew IG: Urinary bladder distension, dilated anus, and atonic tail: the cauda equina syndrome. In Mayhew IG: *Large Animal Neurology: A Handbook for Veterinary Clinicians*, pp 349-357, Philadelphia, 1989, Lea & Febiger.

Scarratt WK, Buechner-Maxwell VA, Karzenski S et al: Urinary incontinence and incoordination in three horses associated with equine protozoal myeloencephalitis. *J Equine Vet Sci* 1999; 19:642-645.

Yvorchuk-St. Jean K: Neuritis of the cauda equina. *Vet Clin North Am Equine Pract* 1987; 3(2):421-428.

CHAPTER 14.7

Idiopathic and Rare Neurologic Diseases

CONSTANZE FINTL
Edinburgh, Scotland

STRINGHALT

Stringhalt is a disease of unknown etiology that has been recognized in horses for centuries. It is characterized by an abnormal gait with involuntary and exaggerated flexion of the hock and stifle of one or both hindlimbs during attempted movement. Stringhalt is typically a disease of individual animals; however, outbreaks have been recorded and are often called Australian stringhalt although outbreaks have also been recorded in New Zealand and North and South America. The classic or sporadic form usually only involves one limb, whereas during outbreaks it often involves both hindlimbs—although one may be more severely affected and even the thoracic limbs can be affected. In its milder form it will usually not limit the performance of the horse, but in the more severe cases it can be a debilitating disease.

Clinical Syndrome

This condition is easily recognizable by the characteristic gait; however, the severity and hence the degree and duration of hyperflexion varies. The severity is often graded from 1 to 5; a grade 1 affected horse displays only mildly exaggerated flexion during backing and turning, and this may disappear during exercise. At the other end of the spectrum, in a grade 5 horse, the fetlock may hit the ventral surface of the abdomen or the point of the elbow during attempted movement. In the case of bilateral stringhalt, forward movement is difficult—especially in the more severely affected cases—and the horse will likely display a plunging, bunny-hopping gait. Involvement of the thoracic limbs is seen as hyperextension and very stiff

movements of the limbs. Rarely, recumbency may result in severely affected horses.

The reason for the characteristic and exaggerated hock flexion is poorly understood, but some have suggested that damage to the reflex arc controlling muscle tone (gamma efferent reflex arc) at one or several points disrupts normal postural tone and coordination of muscle contraction. When damage involves motor fibers to skeletal muscles, it eventually leads to muscle fiber denervation and atrophy.

It is likely that a lesion could exist at any point of the reflex arc or of its connections—that is, it could involve the stretch receptors in the muscle fiber, the afferent nerve, the central nervous system (CNS) synapse, upper motor neuron connections, gamma efferent fibers and muscle spindles, and finally alpha motor axons, the neuromuscular junction, and the muscle itself. In other words, stringhalt may be a consequence of a sensory or motor neuropathy, spinal cord disease, or myopathy.

The cause of either form of this disease has not yet been determined, although previous trauma may be involved in individual cases, whereas a fungal or plant toxicity is suspected where outbreaks occur. Injury to the hock appears to sometimes cause this syndrome—presumably through damage to control of the muscle spindle trigger mechanism. Sometimes after injury, months may elapse before signs of stringhalt develop.

Several studies have tried to identify the pathology of Australian stringhalt outbreaks. This has revealed primary damage to axons in the long peripheral nerves that supply the pelvic limbs. Presumably, small diameter nerve fibers are affected before large diameter motor fibers, thus ac-

counting for the abnormal movement (hyperflexion) before muscle atrophy in the severe cases. The thoracic limbs may also be affected and thus result in stumbling, toe-scuffing, and knuckling at the carpus. Equally, the recurrent laryngeal nerve may also be affected, thus causing laryngeal paralysis and inspiratory stridor.

Diagnosis

The diagnosis of stringhalt is generally easy to make—especially in the more severely affected cases—by observation of the characteristic gait. The challenge is trying to determine the cause because the two forms are clinically indistinguishable.

Most outbreaks have been recorded in late summer or early autumn and are typically associated with droughts and overgrazing on poor pasture. This form of the disease has been recorded in Australia, New Zealand, and North and South America, and repeated outbreaks have occurred on certain pastures. Because the outbreaks tend to occur during certain climatic conditions that favor production of mycotoxins, a mycotoxic cause remains a strong possibility. One plant that has been implicated is *Hypochaeris radicata* (false dandelion), although other plants such as *Taraxacum officinal* have been suggested as a possible source of toxin. Examination of the pasture quality, combined with geographic and meteorologic considerations, are important in establishing a possible cause—especially where it could favor production of mycotoxins. This is important for all cases—not exclusively during outbreaks.

In sporadic cases, careful history taking may help establish a history of previous trauma or injury to the affected hindlimb such as a laceration to the long digital extensor tendon. Often, however, the initiating factor is unknown.

In outbreaks, the onset is sudden. Usually several horses that graze the field will be affected, and the severity may increase during the initial days to weeks. However, in contrast to horses affected by sporadic cases, these horses will generally improve and often fully recover without treatment although this may take months to years. It is unclear whether an age, breed, or sex predilection exists for this condition. However, this appears not to be the case.

Clinical and neurologic examination is generally unrewarding in both sporadic cases and those from an outbreak. Hematologic and biochemistry analysis is equally unrewarding; however, electromyographic recordings of the long digital extensor muscle will often reveal the continuous firing of action potentials. This finding seems to disappear once the animal has recovered.

Because stringhalt may also have a central cause, ruling out other CNS conditions such as equine protozoal myeloencephalopathy (EPM) through collection and analysis of cerebrospinal fluid (CSF) is also important.

Treatment

Few cases of sporadic stringhalt will improve or recover spontaneously given time and rest. However, it is reasonable to investigate whether any underlying orthopedic disease that could account for the observed clinical signs is or was present. It appears that some horses will develop signs of stringhalt after orthopedic conditions that do not nec-

essarily involve the hock or metatarsus. In addition, if stringhalt is already present, the severity may increase in the event of additional orthopedic pain in that limb. In the former group, resolving the underlying orthopedic condition will abolish these signs, whereas for the latter, it may return to a previous degree of severity.

Mildly to moderately affected sporadic cases may improve following tenectomy of a long section of the lateral digital extensor tendon and its musculotendinous junction. This procedure can be performed in the standing horse but also during general anesthesia. Some horses may show immediate improvement after this procedure, whereas others may take weeks to months before any improvement is observed. This procedure may work in some cases by producing changes in the proprioceptive information received centrally from this region of the hindlimb. The inconsistent results of this procedure may be related to the number of different sites where pathology may be present.

Medical treatment options that have been tried include the administration of baclofen and phenytoin. The former is a γ -aminobutyric acid (GABA) receptor agonist which through this effect potentiates the inhibitory neurotransmitter or modulator effect of GABA in the CNS because GABA is one of the most important inhibitory neurotransmitters. It may also alter the perception of proprioceptive information or may act on as yet undetected pathology within the CNS. One study administered 1 mg/kg orally three times daily to ten clinically affected horses; eight horses improved while on treatment. However, seven of these regressed after termination of treatment; three of these subsequently recovered.

Phenytoin was one of the earliest drugs used to treat epilepsy in humans through its effect of reducing neuronal excitability centrally through blocking of sodium and potassium channels. Successful treatment of five long-standing cases of Australian stringhalt with phenytoin (15–25 mg/kg PO q24h for 2 weeks) has been described. The degree of severity was reduced during treatment but again regressed after termination. No signs of toxicity appeared during administration, but some horses appeared to be mildly sedated during administration. Four of these horses recovered spontaneously between 1 and 4 months after the end of the treatment.

These drugs may offer relief for severely affected horses and chronic cases in which the condition is performance-limiting. However, the studies also further support the findings that cases from an outbreak will usually recover, given time.

Given the likelihood of an underlying toxicity to cause stringhalt outbreaks, prevention of the disease is important. If possible, this involves avoiding grazing the animals on poor pastures or pastures with previous cases during the summer and autumn—especially if it has been a dry season. Improving the pasture quality will also be of benefit in helping to prevent outbreaks. Clearly if a diagnosis of EPM has been made, it is another additional treatment option to be pursued.

Prognosis

As previously mentioned, most sporadic cases of stringhalt are unlikely to recover with rest alone. Correction of

any underlying orthopedic process should be undertaken. If the degree of severity of residual signs affects the intended use of the horse the suggested treatment options should be pursued. In the case of stringhalt associated with outbreaks the prognosis is generally favorable; the majority of horses improve significantly or recover fully, although this may take many months to years. The prognosis following surgery in sporadic cases varies, but some horses may show immediate improvement.

SHIVERING

Shivering is a condition of unknown etiology with a suspected genetic origin that has been recognized in draft breeds for centuries. The condition is characterized by involuntary spasmodic muscle tremors that most commonly involve the pelvic limbs and tail. It is generally slowly progressive and hence carries a guarded long-term prognosis, although in many cases signs will plateau. No effective treatment for this condition exists, although dietary changes may improve or stabilize some cases.

Clinical Presentation

This condition typically involves the hindlimbs and tail and is most commonly observed if the horse is asked to back or turn or move over in the stable. In some horses the signs will only be evident during the first few strides, whereas others will produce these signs spontaneously when undisturbed in the stable. Typically, one limb will be raised into a flexed and abducted position and be kept like this while trembling for a few moments before being slowly placed to the ground. Commonly, elevation and quivering of the tail will also be observed and will resolve once the affected hindlimb is placed on the ground.

Rarely, the muscles of the forelimb may be affected; the limb may be thrust forward in full extension with the foot barely touching the ground or raised in a semiflexed abducted position. Muscle trembling will be palpable in the hindlimbs when the affected limb is held off the ground.

Diagnosis

Diagnosis is straightforward when the clinical signs are as well defined as described previously. However, problems may arise if clinical signs are less obvious to the examiner. Sometimes, the only abnormality that may be noted is difficulty in picking up a hindlimb for examination or shoeing. If held gently, it is usually possible to feel mild trembling of the limb. Mild quivering or elevation of the tail may also be observed during this procedure. Sometimes forced flexion of the hock may produce more typical signs in a horse that is otherwise normal. It has also been noted that orthopedic pain that may not originate in the affected limb may result in worsening of the degree of shivering already present.

Occasionally this condition can be mistaken for stringhalt during the period of hock hyperflexion, and cases of equine movement disorders that have characteristics of both stringhalt and shivering certainly have been reported. Equine polysaccharide storage myopathy (EPSM) is a well recognized condition in draft horses, and other breeds and confirmed cases that display signs of shivering have been

reported. Some of these cases will have mildly to markedly elevated serum activities of creatine kinase (CK) and aspartate aminotransferase (AST), but this appears to be an inconsistent finding. Muscle biopsy of type 2 myofibers such as those of the semimembranosus or semitendinosus muscle groups will reveal storage of amylase-resistant complex polysaccharide and/or glycogen within these. The muscle biopsies can be carried out after regional infiltration of local anesthetic around the biopsy site.

Treatment

Unfortunately as yet no well described effective treatment of this potentially crippling condition exists. It is generally assumed to be a slowly progressive condition that will eventually affect the performance of the horse. However, if the animal should suddenly experience deterioration in the degree of shivering, performing a full orthopedic investigation is helpful to determine whether a separate painful condition could result in or exacerbate these signs.

If a diagnosis of EPSM has been made, dietary changes are recommended. This involves decreasing the intake of carbohydrates while increasing the fat to provide energy through oxidation of fatty acids rather than through carbohydrate metabolism. A minimum of 20% to 25% of the total daily calories should be provided from fat. Changing the diet is most likely to have a positive effect in the less advanced cases.

STIFF HORSE SYNDROME

This is a recently recorded condition in the horse; however, it has been recognized in humans for some time as "stiff man syndrome." It is characterized by muscle rigidity and episodic and often violent muscle cramps. This rare condition is likely associated with antibodies being produced against the enzyme glutamic acid decarboxylase (GAD), the enzyme responsible for converting GABA into its active form. The latter is one of the most important inhibitory central neurotransmitters, and a reduction of this will lead to continuous contraction of both agonist and antagonist muscle groups, thus resulting in spasms.

Clinical Signs

The clinical signs may vary in intensity from mild muscle stiffness to sudden and often violent muscle contractions. Onset is generally insidious, and exercise intolerance associated with mild to moderate muscle stiffness may be the only initial clinical sign. This may easily be attributed to exertional rhabdomyolysis with pain on muscle palpation, although muscle enzyme concentrations will remain within normal range. If untreated, the degree of stiffness will likely progress, and episodes of muscle spasms may become apparent. The latter are typically initiated if the animal is startled, but they may occur spontaneously during voluntary movement. In the horse, the axial lumbar and hindlimb muscles are typically involved and may result in an almost laminitic type stance during the more severe episodes. The head and neck may be elevated as well as the tail head. The duration of the spasmodic episodes may vary from a few seconds to minutes. It is likely that a significant degree of

discomfort and pain is associated with these spasms (as there is in man) and hence the animal will often have an anxious expression during these episodes. In humans it is not uncommon for patients to suffer fractures as a result of violent muscle spasms. Between episodes the horse may appear normal, although if present the generalized muscle stiffness may persist. Although only a limited number of cases have been recorded, a breed or sex predisposition does not seem to exist, and no cases have been noted in foals.

Diagnosis

The clinical signs described are based on a low number of recorded cases, and hence although these may be typical they are of course not necessarily complete nor are they pathognomonic for this condition. Clinical examination is generally unremarkable, but pain on palpation of the lumbar and proximal hindlimb musculature may occur. Associated muscle atrophy of these muscle groups does not seem to exist; indeed it has been suggested that these muscle groups may be slightly hypertrophied. A neurologic examination will likely fail to detect any abnormalities apart from the intermittent hyperreflexia.

Few conditions are similar in appearance and presentation to this condition. However, diffuse and multifocal disease of the CNS must be included in the list of differential diagnoses, and a CFS sample should be collected. CSF analysis should include ruling out equine protozoal myelitis (see Chapter 2.11: "Equine Protozoal Myeloencephalitis"). A muscle biopsy is also advisable to rule out peripheral muscle disorders such as EPSM. The tetanus vaccination status of the animal should also be checked, as should the ionized calcium concentration. Strychnine poisoning has also been known to produce similar signs, but a thorough history should help eliminate this possibility.

Hematology and serum biochemistry—including measurements of ionized calcium, AST, CK, and lactate dehydrogenase (LDH) isoenzymes—are generally unremarkable but can help to eliminate rhabdomyolysis from the differential diagnosis list. Because this condition in its milder form may also resemble other muscle disorders, such as EPSM, muscle biopsy of the semimembranosus or semitendinosus muscle is recommended. This can be performed under standing sedation and after infiltration of local anesthesia around the biopsy site. The examination of the biopsy material should include looking for evidence of scattered type-2 myofiber necrosis associated with exertional rhabdomyolysis and for evidence of complex polysaccharide accumulation resistant to amylase digestion consistent with EPSM.

Electromyographic tests may also be performed on the affected muscle groups, which will likely show continuous motor unit activity. This activity appears to be restricted to the affected muscles and is caused by involuntary motor units firing at rest.

Administration of benzodiazepine should in theory reduce or alleviate the severity of the muscle spasms through its ability to potentiate the effect of the GABA already present. An initial dose of 0.05 mg/kg diazepam may be administered by slow intravenous injection. However, some horses may become anxious after intravenous diazepam administration; hence some care during and fol-

lowing this procedure is advisable. Response to this drug appears to vary; thus a tentative diagnosis is supported by detection of antibodies against the enzyme GAD in the serum and in CSF. It may be necessary to arrange with a human hospital for determination of the GAD titer. As this is a rare condition in the horse, the test relies on cross-reaction with human antigens.

Treatment

Given the pathophysiology of the condition, the two main therapeutic options currently available include administration of benzodiazepines and/or immunosuppression. In humans daily doses of diazepam up to 300 mg/day has been prescribed. It follows on from this that in practical terms glucocorticosteroid administration is likely a more realistic medium- to long-term treatment option in the horse. Oral prednisolone administration at immunosuppressive doses of 2 mg/kg/day is indicated, but potential complications are, of course, associated with this therapy—including laminitis. Lower doses may be attempted, but little effect seems to occur at these levels. However, a good response has been reported at immunosuppressive doses. Other treatment options used in humans but not yet tried in equine patients include baclofen and vigabatrin, both of which enhance GABA neurotransmission. Unfortunately, administration of prophylactic analgesics such as nonsteroidal antiinflammatory drugs appears to have little effect in alleviating the discomfort.

Prognosis

The prognosis is generally poor because of the apparent progression of this condition. However, attempts should be made at stabilizing the disease as good responses to immunosuppressive therapy has been recorded. In addition, with the possibility of other therapeutic alternatives becoming available, this may offer further treatment options in the future. However, a welfare implication clearly exists; some of the spasms are likely very painful, and the disease is likely to progress.

Supplemental Readings

- Cahill JI, Goulden BE: Stringhalt: current thoughts on aetiology and pathogenesis. *Equine Vet J* 1992; 24:161-162.
- Huntingdon PJ, Seneque S, Slocombe RF et al: Use of phenytoin to treat horses with Australian stringhalt. *Aust Vet J* 1991; 68:221-224.
- Kannegieter NJ, Malik R: The use of baclofen in the treatment of stringhalt. *Aust Equine Vet* 1992; 10:90.
- Mayhew IG: Stringhalt, lathyrism and shivering. In Mayhew IG: *Large Animal Neurology: A Handbook for Veterinary Clinicians*, pp 219-220, Philadelphia, Lea & Febiger, 1989.
- Nollet H, Vanderstraeten G, Sustronck B et al: Suspected case of stiff-horse syndrome. *Vet Rec* 2000; 146:282-284.
- Valentine BA, de Lahunta A, Divers TJ et al: Clinical and pathologic findings in two draft horses with progressive muscle atrophy, neuromuscular weakness, and abnormal gait characteristic of shivers syndrome. *J Am Vet Med Assoc* 1999; 215:1661-1665.

CHAPTER 14.8

Changes in Mentation, Seizures, and Narcolepsy

MELISSA TROGDON HINES

Pullman, Washington

The forebrain—which includes the telencephalon (cerebral cortex and basal nuclei) and diencephalon (hypothalamus, thalamus, subthalamus, and metathalamus)—provides the primary control of mentation and behavior. Of particular importance is the cerebral cortex, which comprises the frontal, parietal, occipital, and temporal lobes, and the thalamus. The cerebral cortex contributes to several critical functions—including consciousness, complex behavior, fine motor activities, processing sensory information, and vision. Parts of the temporal and frontal lobes are included in the limbic system, which is responsible for many emotions and innate survival behaviors, such as the protective maternal response. The thalamus functions with the cerebrum as a unit to maintain consciousness and acts as a relay center through which sensory information from the periphery reaches the cerebrum and motor impulses from the cerebrum reach the brainstem motor centers. In particular, neuronal pathways of the ascending reticular activating system (ARAS) project from the midbrain through the thalamus diffusely to the cerebral cortex, thus helping to maintain the level of consciousness.

CLINICAL SIGNS OF FOREBRAIN DISEASE

The nature and severity of clinical signs seen with forebrain disease vary by the location and extent of the disorder. The complex interrelating functions make precisely localizing the lesion within the cerebrum or thalamus difficult. The most commonly observed sign associated with forebrain disease is a change in mental status. In most cases, this is a decrease in alertness that ranges in severity from mild dullness and depression to obtundation, stupor, and coma. Lesions that involve the ARAS tend to cause particularly severe depression of consciousness, such as stupor or coma. Rather than decreased alertness, certain forebrain lesions result in increased responsiveness to external stimuli, anxiety, mania, or aggression. Lesions of the limbic system are especially prone to cause these behavioral changes.

A variety of signs in addition to changes in mentation may be seen with forebrain disease. The signs can vary, depending on whether the condition is diffuse or focal. Diffuse conditions, such as those caused by metabolic or toxic disorders, affect the whole forebrain. Focal problems, such as neoplasia or abscessation, result in asymmetric clinical signs. Compulsive walking may be observed. In

the presence of focal asymmetric disease, the horse tends to circle toward the side of the lesion. With diffuse disease, circling does not generally occur. The severity of the circling varies from a slight tendency to drift to obvious circling but is not as compulsive as that seen with lesions of the midbrain. Horses with asymmetric lesions may turn their heads to the side of the lesion but do not have a head tilt, nystagmus, or strabismus as is seen with problems that originate in the vestibular system.

Movements that require visual input or complex integration of limb and body movements initiated in the motor centers of the cerebral cortex are affected by forebrain disease. The gait generally appears normal on a level surface but can be abnormal when the horse performs more complex maneuvers, such as circling, backing up, and negotiating a slope or obstacles. Although both ataxia and paresis can be present, ataxia is most prominent. Postural and proprioceptive reflexes and reactions are abnormal. In the case of asymmetric lesions, gait deficits of varying severity are seen in the contralateral limbs.

The response to visual stimuli, which may be assessed by the menace response, is diminished or absent because of involvement of visual pathways in cerebral cortex. However, pupillary light responses are normal except in severe cases in which the oculomotor nerves are subject to damage from diffuse cerebral swelling or space-occupying lesions in the forebrain. In cases of asymmetric cerebral swelling, dilation of the ipsilateral pupil may be seen.

Response to sensory input to the cerebrum may decrease, primarily with involvement of the parietal (sensory) lobe. This is particularly evident as a facial hypalgesia, which is observed on the contralateral side with asymmetric lesions. The variable severity of the hypalgesia helps to differentiate it from specific cranial nerve deficits in which the horse's mental status is normal and the deficit tends to be more severe. With extensive forebrain lesions, horses may also fail to retract the tongue when it is pulled from the mouth, although they can do so during vigorous stimulation. Because the higher motor centers control facial movement, hypertonicity and hyperreflexia of the facial muscles that are manifested as facial grimacing can occasionally be seen with focal thalamic and cerebral lesions in horses.

Seizures are another sign of cerebral disease, and they are commonly seen in conjunction with other neurologic abnormalities. Also known as a convulsion, ictus, or fit, a seizure is a physical manifestation of spontaneous parox-

ysmal electrical activity in the cerebral cortex. Ultimately, seizures are a sign of cerebral cortical dysfunction, although the activity may be initiated elsewhere and spread to the cerebrum. Seizures are characterized by a loss of consciousness and/or involuntary motor activities and may be focal (partial), generalized, or focal with secondary generalization. Generalized seizures are associated with a loss of consciousness, collapse, and variable degrees of tonic-clonic motor activity. In the case of focal seizures, involvement of a small number of neurons results in localized involuntary movements with or without obvious alterations of consciousness. Common signs of abnormal motor activity associated with focal seizures include muscle twitching in the face or one limb, grimacing, and head-turning. Occasionally, focal seizures may result in episodes of abnormal behavior or short lapses of consciousness without significant motor activity. In most animals with focal seizures, the outward manifestation remains consistent. In the case of focal seizures with secondary generalization, the activity spreads from a focal site throughout the cerebral cortex, thus resulting in generalized seizures.

The aura is the time period immediately preceding a seizure in which some individuals exhibit behavioral changes such as anxiety or restlessness. In many cases, an aura is not recognized. The time period subsequent to the seizure—the postictal phase—is also characterized by behavioral changes such as lethargy, restlessness, and anxiety. Some horses may have temporary blindness. Generally, the postictal phase lasts minutes to hours but occasionally lasts several days. In some cases, the seizure is never observed and is only suspected on the basis of postictal behavioral changes or the presence of repeated physical injuries.

DISEASES THAT MANIFEST WITH SIGNS OF FOREBRAIN DISEASE

Clinical forebrain disease may result from either intracranial causes, such as encephalitis or trauma, or extracranial causes, such as toxicities or metabolic disorders. Changes in mentation and behavior have been seen in association with a wide variety of disease conditions (Box 14.8-1). With some disorders, such as hepatic encephalopathy and eastern equine encephalomyelitis (see Chapter 2.5: “Viral Encephalitides”), cerebral signs predominate, whereas with other disorders, such as equine protozoal myeloencephalitis (EPM, see Chapter 2.11: “Equine Protozoal Myeloencephalitis”) and equine herpesvirus type 1 (EHV-1, see Chapter 2.2: “Equine Herpesvirus”), the presentation may vary and does not always include cerebral signs.

Trauma

The signs of traumatic brain injury generally result from hemorrhage, cerebral edema, and increased intracranial pressure. The clinical signs will vary somewhat by the precise site and degree of injury and may be asymmetric.

Hepatic Encephalopathy

Hepatic encephalopathy is a clinical syndrome characterized by abnormal mental status that occurs secondary to

BOX 14.8-1

Conditions Associated with Signs of Forebrain Disease

Trauma
Hepatic encephalopathy
Leukoencephalomalacia
Viral encephalitides
 West Nile virus meningoencephalitis
 Rabies
 Equine herpes myeloencephalopathy
 Equine protozoal myeloencephalitis
Brain abscesses
Brain tumors
Verminous encephalitis
Locoweed intoxication
Meningitis
Hypoxic ischemic encephalopathy
Hydrocephalus
Metabolic abnormalities
Rare causes
 Equine infectious anemia virus
 Persistent hyperammonemia of Morgan foals

hepatic insufficiency. Although the precise pathophysiology of hepatic encephalopathy remains undefined, the syndrome is probably multifactorial. The following three major mechanisms have been proposed: (1) accumulation of neurotoxins, primarily ammonia; (2) accumulation of false neurotransmitters due to decreased metabolism of aromatic amino acids; and (3) increased activity of the inhibitory neurotransmitter, gamma-aminobutyric acid (GABA).

Clinical signs of hepatic encephalopathy are generally characteristic of cerebral dysfunction. Early in the course of the disease, signs may be subtle and nonspecific. The predominant sign is a change in behavior, which is generally seen as depression, although occasionally horses become excitable and difficult to control. Yawning is sometimes seen in horses. Rarely inspiratory stridor due to laryngeal paralysis has been observed, but the exact pathogenesis is unknown.

Leukoencephalomalacia (Moldy Corn Disease, Equine Encephalomalacia, Blind Staggers)

Leukoencephalomalacia is an intoxication of horses caused by ingestion of corn contaminated with the fungus *Fusarium moniliforme*, which may produce fumonisin toxins (B1, B2, and B3). Whereas the pathophysiology is not fully understood, the primary mycotoxin is felt to be fumonisin B1 (FB1), which interferes with sphingolipid metabolism disrupting endothelial cell walls and basement membranes. The damage leads to liquefactive necrosis and degeneration or malacia of the white matter of one or both cerebral hemispheres. Lesions may also be seen in other tissues, primarily the liver.

Leukoencephalomalacia is seen worldwide, with most cases occurring in winter and early spring. Typically there

is an acute onset of signs 3 to 4 weeks after daily ingestion of contaminated feed. In some cases, the feed source is elusive, and the disease has been recognized with commercial feeds as well as corn. Also, not all moldy corn contains the toxin. The disorder may occur as an outbreak, with 14% to 100% of animals affected, and generally older horses appear to be most susceptible. The primary clinical syndrome is neurotoxicosis, although hepatotoxicosis is recognized in some horses.

Alphavirus and Flavivirus Encephalitis

Several viruses in the *Togaviridae* family are important causes of equine neurologic disease (see Chapter 2.5: “Viral Encephalitides”). These viruses generally infect sylvatic hosts—such as wild birds, small mammals, and reptiles. As arboviruses, they are transmitted by insect vectors, which can also spread the viruses to other animals, such as horses and human beings. Until recently, members of the alphavirus genus—including eastern equine encephalomyelitis (EEE), western equine encephalomyelitis (WEE) and Venezuelan equine encephalomyelitis (VEE)—were considered the most significant. In 1999, West Nile virus (WNV), a flavivirus, was first recognized in North America as a cause of disease in crows, human beings, and horses in New York. Since that time, the disease has spread rapidly, and in 2001, there were over 700 recorded cases of WNV in horses. Other flaviviruses—including Japanese B encephalitis, California encephalitis (snow-shoe hare encephalitis), St. Louis encephalitis, Murray Valley encephalitis, Cache Valley virus, Main Drain virus, and others—have also been sporadically associated with equine encephalitis.

Equine, Western, and Venezuelan Encephalitis (Equine Sleeping Sickness)

The alphaviral encephalitides—EEE, WEE, and VEE—are generally associated with fever and mild depression in the early stages. Affected horses may then develop signs related to diffuse encephalitis. Typically, EEE is the most severe clinically, and in some cases sudden death may be seen. WEE is milder and may not progress beyond the nonspecific signs. The clinical signs of VEE are variable and nonneurologic signs—such as oral ulcers, diarrhea, pulmonary hemorrhage and epistaxis—may be seen. The horse is generally a dead end host for both EEE and WEE. However, in the case of VEE, horses can develop sufficient viremia to act as amplifiers of the disease.

West Nile Virus Meningomyeloencephalitis

The avian host range for WNV is broad; several species of birds serve as amplifying hosts. Also, several genera of mosquitoes can become infected by feeding on viremic birds and are able to transmit the virus. In horses, most infections with WNV result in subclinical or mild disease, but about 10% of infected horses will develop severe clinical signs. Infected horses are often depressed, eat poorly, and may have fevers. Muscle fasciculations and hyperesthesia may be observed. Changes in mentation often occur, and horses may go from being apprehensive and overly responsive to extremely dull. However, convulsions and coma are rare. In comparison to EEE, horses with WNV are more likely to ex-

hibit weakness and spinal ataxia. Paralysis of the lips and tongue are also seen.

Rabies

The rabies virus is a highly neurotropic Rhabdovirus that causes fatal neurologic disease (see Chapter 2.5: “Viral Encephalitides”). Although rabies is relatively uncommon in horses, it should be considered a differential diagnosis in horses with neurologic disease because of the zoonotic potential. The virus is transmitted primarily through saliva-contaminated wounds. In horses, the most common route of infection is a bite wound from a wild carnivore or bat carrying the virus, although the source of infection is usually not apparent, partially because the incubation period can vary from 9 days up to 1 year.

Clinical signs of rabies are highly variable. Initial signs often include hyperesthesia, colic, self-mutilation, or apparent lameness. Fever may or may not be present. Behavioral changes include either marked depression, as in the dumb form, or extreme hyperexcitability, fear, and aggression, as in the furious form. Gait deficits, including ataxia and paresis, are common. Typically, clinical signs progress rapidly, and death occurs within 5 to 10 days of the onset of clinical signs.

Equine Herpesvirus Myeloencephalopathy

EHV-1 may be associated with a variety of neurologic signs (see Chapter 2.2: “Equine Herpesvirus”). Although the most common abnormalities include ataxia and paresis with bladder atony and decreased tail and anal tone, signs of cerebral disease may be observed.

Equine Protozoal Myeloencephalitis

EPM is caused primarily by infection with *Sarcocystis neurona* (see Chapter 2.11: “Equine Protozoal Myeloencephalitis”). In rare cases, *Neospora* species have been implicated. The protozoa cause inflammation and necrosis within the central nervous system; affected horses exhibit a wide variety of signs, depending on the location of the parasite damage. Although spinal cord signs are probably most common, a variety of cerebral signs, including behavioral changes and seizures, have been reported. Signs may be either asymmetric or symmetric.

Brain Abscesses

Intracranial abscesses—caused either by direct extension from trauma and skull fracture or hematogenous spread—have been reported in both foals and adult horses. Although the number of reported cases is small, *Streptococcus equi* subspecies *equi* appears to be common. Signs vary by the precise location and size of the abscess and are often asymmetric. Vision loss in the contralateral eye and generalized cortical signs—such as depression, circling, and seizures—are common.

Brain Tumors

Both primary and metastatic neoplasms have been reported in the central nervous system of horses, although

they are infrequent. Lymphosarcoma is the most common metastatic tumor. The clinical signs vary with the location of the mass.

Cholesteatomas, which are cholesterol granulomas, are common in older horses but are generally asymptomatic. Occasionally, they may cause signs of cerebral dysfunction by obstruction of CSF flow or rarely by attenuating the surrounding neuropil directly.

Verminous Encephalitis

Verminous encephalitis and myelitis occur sporadically in horses. As parasites may migrate randomly, signs can reflect focal or diffuse brain or spinal cord involvement. Several parasites have been reported—including *Strongylus*, *Hypoderma*, *Habronema*, *Draschia*, and *Setaria* species. *Hali- cephalobus gingivalis* (*H. deletrix*, *Micronema deletrix*) is a ubiquitous saprophytic nematode reported to infect human beings and horses. The nematode may form granulomas in the integument or may disseminate, with a predilection for the CNS and kidneys. Transmission of *H. gingivalis* from dam to foal has been reported. Rarely, parasitic thromboembolism associated with *Strongylus vulgaris* thromboarthritis may lead to an embolic shower to the cerebrum.

Locoweed Intoxication

Ingestion of certain species of the plants *Astragalus* and *Oxytropis* may induce locoism. The toxic components of locoweeds are thought to be the indolizidine alkaloids—swainsonine and swainsonine N-oxide. These alkaloids inhibit alpha-mannosidase, thus resulting in the accumulation of mannose-rich oligosaccharides in lysosomes, seen as intracytoplasmic vacuoles in a variety of tissues. These vacuoles disrupt cellular function. In the nervous system, they are found predominantly in cells of the cerebral cortex and cerebellum. The onset of clinical signs varies from 2 weeks to 2 months after the horse starts to graze the plants. Typical clinical signs include depression, nervousness, aggressive behavior, ataxia, and weight loss. Affected horses may also have trouble eating and drinking as well. Because of the number of tissues that can be affected, a variety of other signs may be seen in addition to the neurologic abnormalities.

Meningitis

Meningitis may occur either as a result of direct extension of infectious agents into the calvarium or from hematogenous infection. Direct extension can occur in association with skull fractures, sinusitis, otitis media-interna, and guttural pouch disease. Hematogenous spread is most common in neonates in association with septicemia. Most cases are bacterial in origin, although fungal meningitis may occur as well.

Hypoxic-Ischemic Encephalopathy (Neonatal Encephalopathy)

Hypoxic-ischemic encephalopathy (HIE), previously known as *neonatal maladjustment syndrome* or *dummy foal syndrome*, is one of the most common problems of the

equine neonate (see Chapter 12.4: “Perinatal Asphyxia Syndrome in Foals”). Although the precise mechanisms of cellular damage in HIE are still unclear, asphyxia leads to a cascade of inflammatory and neurochemical changes that result in neuronal cell death. Most often, affected foals are normal at birth but begin to show signs within a few hours, although the age of onset ranges from birth to around 24 hours of age. A spectrum of clinical signs are associated with HIE and range from mild depression and decreased suckling to seizures.

Hydrocephalus

Hydrocephalus, an accumulation of cerebrospinal fluid within the ventricles of the brain, is rare in horses. It is most often seen in neonatal foals as a congenital malformation. Occasionally, hydrocephalus is acquired in foals secondary to meningitis or hemorrhage. The exact cause of congenital hydrocephalus in foals is unknown but in some cases is suspected to be heritable. The head may be grossly enlarged and dome-shaped, but this is not always apparent. Also, a dome-shaped skull is more often an indication of immaturity or intrauterine growth retardation. Signs of hydrocephalus vary in severity, although the condition is generally fatal.

Metabolic Causes

A variety of metabolic derangements have been associated with CNS abnormalities, particularly in neonatal foals. These include hypoglycemia, acidosis, hyponatremia or hypernatremia, hypocalcemia, and hypomagnesemia.

Other Causes

Infection with equine infectious anemia (EIA) virus infrequently causes a granulomatous ependymitis, choroiditis, meningitis, and encephalomyelitis. Encephalitis associated with *Borrelia burgdorferi* infection has been reported in a horse; however, the actual significance of this organism in horses has not been confirmed. Encephalopathy associated with persistent hyperammonemia was reported in two Morgan fillies in association with a probable inherited metabolic disorder. Horses with marked azotemia may occasionally present with signs of encephalopathy.

DIAGNOSTIC APPROACH TO FOREBRAIN DISEASE

Signalment and History

Certain elements of the signalment and history may help to prioritize the differentials for forebrain disease. Disorders such as meningitis, HIE, hydrocephalus, and metabolic derangements are most often recognized in neonatal foals. Neoplasms are most common in adult horses, although they are not limited to geriatric individuals. Older horses also appear most susceptible to leukoencephalomalacia. In Morgan foals with cerebral signs, persistent hyperammonemia should be considered.

The geographic location and travel history should be considered because many diseases have a regional distribution.

In the United States, EEE is found primarily in the East and is particularly common in the southeast. WEE has been seen throughout the United States but is more common in the West. The last epizootic of VEE in the United States was in Texas in 1971. WNV, now recognized in 27 states, is rapidly expanding its range from the eastern seaboard. Also, the arboviral encephalitides have a seasonal incidence corresponding to the vector season. Diseases such as rabies and EPM are less common in some regions, such as areas of the Pacific Northwest. Locoweeds extend southward from western Canada to include the western United States and northern Mexico.

Exposure to tetanus antitoxin or hepatotoxic plants, such as pyrrolizidine-containing plants (*Senecio*, *Amsinckia*, *Crotalaria*, *Eichium*, *Heliotropium*, and *Cynoglossum* spp.) or alsike clover, increases the likelihood of hepatic encephalopathy. Leukoencephalomalacia, which is linked to exposure to moldy corn or feed, may be associated with a dry growing period followed by a wet period and is most often seen from late fall through early spring. Conditions that may involve more than one horse include hepatic encephalopathy, leukoencephalomalacia, locoism, and EHV-1. In some cases of EHV-1, horses will have a history of recent respiratory disease.

Clinical Signs

Physical and neurologic exam findings can be helpful in determining the etiology of forebrain disease. The presence of bleeding from the nares, external ear canal, or guttural pouch is supportive of trauma. Although not a consistent finding, fever is suggestive of an infectious etiology. Horses with hepatic encephalopathy—and sometimes with leukoencephalomalacia—may have signs of liver dysfunction other than neurologic signs—including icterus, anorexia, weight loss, and photosensitization. Rabies and EEE tend to be severe and rapidly progressive.

Hematology

A complete blood count (CBC) and fibrinogen may yield useful information in cases of forebrain disease but will not establish a specific diagnosis. Nonspecific changes associated with dehydration or stress may be seen. In cases of viral disease, a neutropenia and lymphopenia may be detected in the early stages but is not consistent. Occasionally, eosinophilia is seen in association with verminous encephalitis. Findings are variable in cases of meningitis, with either leukocytosis or leukopenia with a left shift and toxic changes. Brain abscesses may be associated with changes typical of chronic infection—including anemia, hyperfibrinogenemia, hyperproteinemia due to hyperglobulinemia, and neutrophilia. Rarely, intracytoplasmic vacuoles are seen in circulating lymphocytes in cases of locoism.

Serum Chemistry

A serum chemistry profile and blood gas analysis help to rule out metabolic causes of changes in mentation. Changes consistent with liver dysfunction—including elevations in liver enzymes, bilirubin, serum bile acids, and

blood ammonia—are found in hepatic encephalopathy. Liver disease may also be associated with clotting abnormalities, and in severe cases, decreased albumin and blood urea nitrogen (BUN). Hypoglycemia may be seen, particularly in foals with marked hepatic insufficiency. Abnormalities consistent with liver disease may be seen in some cases of leukoencephalomalacia. Persistent hyperammonemia and variable elevations of hepatic serum biochemical values and function tests have been seen in Morgan foals. Hypercalcemia may support the possibility of neoplasia or renal disease. If significant azotemia is present, uremic encephalopathy should be considered.

Analysis of Cerebrospinal Fluid

Analysis of cerebrospinal fluid (CSF) may be helpful in establishing the diagnosis of forebrain disease. Because of the risk of brainstem herniation, collection from the atlantooccipital cistern may be contraindicated if signs of increased CSF pressure—such as mydriasis, blindness, papilledema, or uncontrolled hemorrhage from the ears or nose—occur.

The presence of blood in the CSF suggests either contamination during sample collection or trauma. Xanthochromia, a yellowish discoloration, is frequently associated with previous hemorrhage and may also be seen with significant elevations of protein or bilirubin in the CSF. Following trauma, xanthochromia may be present for up to 14 days. Xanthochromia has also been commonly reported with EHV-1 myeloencephalopathy and—in some cases of HIE—rabies, meningitis, and verminous encephalitis.

A number of conditions may cause an increase in cells and protein in the CSF. Although individual laboratory values may vary somewhat, normal equine CSF typically has a total protein of 20 to 124 mg/dl and less than 10 nucleated cells/L, which are predominantly mononuclear cells. Significant increases in neutrophils and protein are associated with the alphavirus encephalitides—especially EEE—and septic meningitis. White blood cells counts may reach more than 100,000 cells/ μ l and be sufficient to make the CSF appear grossly turbid. Infrequently, mononuclear cells rather than neutrophils may predominate. Organisms may be seen in some cases of septic meningitis, and the glucose may be low. Although the neutrophil count can be increased with brain abscesses, the CSF is often normal. Culture of the CSF is warranted if infection is suspected. In contrast to EEE, the CSF in cases of rabies is typically normal or has only moderate increases in mononuclear cells and protein. The CSF is highly variable with WNV and may be normal or may have increases in mononuclear cells and protein. In the case of EHV-1, the CSF may be normal or increased protein with a normal or only slightly increased nucleated cell count may occur. The CSF is most often normal with EPM, but in about 15% of cases a mononuclear nonsuppurative pleocytosis occurs. In cases of verminous encephalitis, the CSF is generally normal, although occasionally an eosinophilic or neutrophilic leukocytosis is seen. Rarely, *H. gingivalis* may be identified in the CSF. The diagnosis of CNS neoplasia can be confirmed by the presence of neoplastic cells; however, these cells are not present in most cases.

Serology

A number of serologic tests are available for the diagnosis of infectious disorders. In the case of EIA, the presence of antibody indicates the presence of virus, except in young foals, in which passive transfer of antibody may cause transiently positive readings. For many other infections, the presence of antibody indicates exposure, infection or vaccination. In general, a fourfold or greater rise in titer suggests recent infection; however, the timing of sample collection may affect the results. In diseases with a rapid rise in antibody, the initial sample may be taken when antibody levels have already peaked.

Antibodies, particularly IgM, tend to rise rapidly after infection with EEE, WEE, VEE, and WNV. A number of assays—including hemagglutination inhibition, virus neutralization and IgM and IgG capture enzyme-linked immunosorbent assays (ELISAs)—have been used in the diagnosis of EEE, WEE, and VEE. Identifying a rise in titer, viral induced IgM, and comparing titers for EEE and WEE may help to differentiate titers due to infection from those due to vaccination. Currently, the IgM capture ELISA is considered the optimal test for *ante mortem* diagnosis of WNV infection.

Serologic testing is also considered valuable in the diagnosis of EHV-1 myeloencephalopathy. A fourfold rise in the serum neutralizing antibody titer or a single titer of 1:256 or higher is suggestive of recent infection. A complement fixation (CF) titer of 1:16 is considered consistent with recent infection, but because these titers decline rapidly after infection, identifying a rise in the CF titer is often difficult. The presence of antibodies to EHV-1 in the CSF strongly suggests the diagnosis, but these antibodies are absent in many cases.

Antibodies specific for *S. neurona* are currently detected in the serum or CSF by the Western blot test. Many normal horses have serum antibodies specific for *S. neurona* due to the high rate of exposure. However, it is uncommon for horses infected with *S. neurona* to have a negative Western blot, and in those regions with a low prevalence of EPM, serologic testing may be used as a screening tool. The presence of antibodies for *S. neurona* in the CSF is supportive of EPM but does not confirm the diagnosis.

Diagnostic Imaging

Diagnostic imaging techniques can be useful in identifying certain intracranial disorders. Some skull fractures can be diagnosed by radiography. Computed tomography and magnetic resonance imaging have been diagnostic in cases of trauma, brain abscesses or tumors, and hydrocephalus.

Other Diagnostic Procedures

Additional ancillary diagnostic tests may be useful. Feed can be analyzed for the presence of toxic plants and for the FB1 toxin, which should not exceed 5 to 10 ppm. In cases of hepatic encephalopathy, ultrasound and biopsy of the liver may help confirm the diagnosis. Viral isolation from the buffy coat or nasopharyngeal swabs may help establish a diagnosis of EHV-1, although viral isolation from the CSF is unrewarding. Identification of the encephalitis viruses by viral isolation or polymerase chain reaction may be useful. In many cases of cerebral disease, the diagnosis is established by necropsy. This is true for rabies, in which the diagnosis is confirmed by the presence of Negri bodies and indirect fluorescent antibody staining of tissues.

TREATMENT AND PROGNOSIS

Good supportive care is essential in the treatment of horses with cerebral disease, especially because no specific therapy exists for many conditions. This includes maintaining adequate hydration and nutritional support in those patients that are unable or unwilling to eat and drink and preventing decubital ulcers in recumbent horses. Some horses may benefit from support with a sling. Sedation may be indicated in horses that are extremely anxious or intractable. Acepromazine, xylazine, and detomidine should be used with caution because they may infrequently exacerbate neurologic signs. Controlling seizures with anticonvulsant drugs is critical (Table 14.8-1). Diazepam is often used for short-term control in foals. Long-term control is most often achieved with phenobarbital.

The optimal treatment for skull trauma remains controversial despite the importance of the problem in human

Table 14.8-1
Commonly Used Anticonvulsant Drugs

Drug	Dosage	Route of Administration	Frequency of Administration
diazepam (Valium)	0.01-0.40 mg/kg	IV	q30min as needed to control seizures
phenobarbital			
Initial treatment	12-20 mg/kg initial dose (diluted in saline over 30 min), then 1-9 mg/kg	IV	q8-12h after initial dose
Maintenance	5-11 mg/kg (recommended therapeutic trough concentrations = 15-40 µg/ml)	PO	q12-24h
pentobarbital	2-20 mg/kg	IV	q4h as needed to control seizures

IV, Intravenous; q30min, every 30 minutes; q8-12h, every 8 to 12 hours; PO, by mouth.

medicine. Early recognition and control of increased CSF pressure is important. In some cases, especially those with depression fractures of the frontal and parietal bones, surgical intervention may be warranted.

A number of drugs have been used to decrease the cerebral edema seen in association with trauma and conditions such as HIE—including corticosteroids, dimethyl sulfoxide (DMSO), mannitol, and furosemide (Table 14.8-2). These drugs are probably most effective if given early in the course of the disease, and even then their benefit remains unclear. Drugs are often used in combination, particularly corticosteroids and DMSO as well as furosemide and mannitol. Although dexamethasone is probably the most commonly used corticosteroid in horses with neurologic disease, some data in other species suggest that high-dose methylprednisolone is more effective in improving recovery. The use of mannitol is increasing, particularly in foals. Because its osmotic activity can increase plasma volume, mannitol may potentiate further bleeding in cases with active hemorrhage. Nonsteroidal antiinflammatory drugs may be of some benefit in decreasing inflammation and edema within the CNS.

Cases of hepatic encephalopathy are treated by supportive care and in some cases by treatment of the underlying liver condition. Exposure to any hepatotoxins should be removed. Symptomatic treatment includes feeding a diet low in protein and high in carbohydrates. Optimally, the protein source should be rich in branched chain amino acids. Administration of glucose may be beneficial in some cases. Although their efficacy has not been established, several therapies are directed at decreasing the production or absorption of toxic protein metabolites by enteric bacteria. These include the administration of a poorly absorbable oral antibiotic such as neomycin, lactulose, or mineral oil. Affected horses should be protected from the

sunlight to limit damage from photosensitization. The prognosis is guarded for liver disease in which hepatic encephalopathy is seen.

Other than eliminating exposure to the affected feed source, no specific therapy for either leukoencephalomalacia or locoism exists. Treatment with thiamine has been used in cases of leukoencephalomalacia, however the prognosis is poor; most horses die within hours to days of the onset of clinical signs. Horses occasionally survive with residual neurologic deficits. Signs of locoism may be reversible if ingestion of the toxic plants ceases early in the course of the disease, but typically the disease is chronic and in some cases fatal.

No specific treatment for the viral encephalitides exists. Antiinflammatories—including nonsteroidal antiinflammatories, DMSO, and glucocorticoids—have been used. Mannitol has also been used, especially in severe cases of WNV. Mortality ranges from approximately 20% for WEE, to 40% to 80% for VEE, and 75% to 100% for EEE. Surviving horses may have residual neurologic deficits. In recent studies of WNV, approximately 70% of horses have made a full recovery.

The management of horses with EHV-1 myeloencephalopathy and EPM is discussed in Chapters 2.2 and 2.11, respectively. In the case of EHV-1, the use of antiinflammatory drugs, particularly corticosteroids, is common. Antiviral treatment with acyclovir has been attempted. Horses with EHV generally have a good prognosis if they are not recumbent. Currently the approved therapy for EPM is the antiprotozoal agent ponazuril (5 mg/kg PO q24h for 28 days). Some adjunct therapies include use of antiinflammatory drugs, immunomodulators, and vitamin E. The prognosis for EPM is variable by duration and severity of the disease, and the condition may relapse.

Intracranial abscesses may be treated with long-term antibiotic therapy. Craniotomy for surgical debridement and drainage may increase the success of treatment in selected cases. In the case of meningitis, aggressive antibiotic therapy—ideally based on culture and sensitivity—is indicated. Some antibiotics with good penetration into the CSF include doxycycline, erythromycin, azithromycin, chloramphenicol, metronidazole, trimethoprim-sulfonamide, quinolones, ceftiofur, and cefotaxime. Occasionally intrathecal antibiotics are used. Concurrent use of glucocorticoids may decrease inflammation, although their use is controversial. In cases of verminous encephalitis, antiparasitic and antiinflammatory treatment may be beneficial.

PREVENTION

Vector abatement via elimination of mosquito breeding sites and application of insecticides is beneficial in the control of arboviruses—including EEE, WEE, VEE, and WNV. Housing horses at night and selection of pastures may also help limit exposure to vectors. Vaccination for EEE, WEE, and VEE is effective in preventing disease, and horses in temperate climates should be vaccinated semiannually. A vaccine for WNV is available, and the efficacy is currently under investigation.

Inactivated vaccines for rabies are currently approved for use in horses. In the case of EHV-1, current vaccines do not appear to protect against the neurologic form of

Table 14.8-2

Drugs Used to Control Cerebrocortical Edema

Drug	Dosage	Route
dexamethasone	0.1-0.25 mg/kg q6-24h (typically for 24-48 hours)	IV
methylprednisolone	a. 30 mg/kg followed by 15 mg/kg 2 and 6 hours later, followed by a constant infusion of 2.5 mg/kg/hr for 48 hr	IV
DMSO	b. 100-1000 mg 1.0 g/kg; 10%-20% solution q12-24h	IV
mannitol	0.25-2 g/kg; 20% solution q12-24h	IV
furosemide	1 mg/kg q12h	IV/IM/SQ

q6-24h, Every 6 to 24 hours; IV, intravenous; DMSO, dimethyl sulfoxide; IM, intramuscular; SQ, subcutaneous.

the disease. However, vaccines may reduce shedding and general exposure to virus. Isolating new arrivals, maintaining distinct herd groups, and minimizing stress may help in the prevention of disease caused by EHV-1.

Decreasing exposure to opossum feces may diminish the risk of EPM. A vaccine is available, but the efficacy is still not documented.

SEIZURES

Seizures result from abnormal electrical activity in the cerebrum, as previously discussed. They should be differentiated from other causes of collapse and thrashing, such as narcolepsy, syncope, hyperkalemic periodic paralysis, or painful conditions such as colic or myopathy. Although seizures may be subtle, particularly in foals, they can often be identified by the clinical appearance of the episode and the presence of postictal changes. In some cases, electroencephalography can help to confirm functional disturbances in brain activity.

Seizures may result from a variety of causes, including metabolic abnormalities, structural brain diseases, and inflammatory conditions. In comparison to adult horses, foals appear to have a lower seizure threshold, thus making them more susceptible to conditions that cause seizures. Because seizures are caused by cerebral dysfunction, they can be associated with all of the previously described conditions affecting the forebrain. With most of these disorders, the seizures occur in conjunction with other signs of cerebral disease, but occasionally seizures may be the only manifestation of the problem.

Epilepsy is defined as recurrent seizures, and the term is often expanded to indicate recurrent seizures of unknown etiology. Seizures have been seen in adult horses without an apparent underlying disease process. A syndrome of benign epilepsy has been recognized in foals up to 12 months of age. It is predominantly seen in foals of Arabian breeding. Depending on the frequency and severity of the seizures, affected foals may temporarily require anticonvulsant therapy, but they outgrow the condition.

NARCOLEPSY

The sleep disorder narcolepsy has been recognized in several breeds of horses. Two syndromes of equine narcolepsy appear to exist—the first in which animals are affected at or within a few days of birth and the second in which animals are first affected as adults. The characteristic clinical signs of narcolepsy include excessive sleepiness and cataplexy (muscle weakness, hypotonia). Affected horses exhibit intermittent episodes typically characterized by a gradual lowering of the head followed by buckling of the forelimbs. Repeated episodes often result in abrasions on the front of the fetlocks. Adult horses only occasionally collapse completely and enter rapid eye movement sleep, but this is observed more frequently in foals. Although episodes in adult horses have been reported in association with activities such as feeding, tying in the wash rack, or saddling, no particular inciting event is usually present. In foals, episodes are often triggered by restraint. Although the problem is uncommon, narcoleptic horses have been reported to collapse while being ridden.

The pathogenesis of narcolepsy in horses is not fully understood. Some evidence suggests a genetic basis in dogs and humans, and familial narcolepsy has been reported in Miniature Horse foals. The physiologic control of sleep is complex. Neuropeptides located in the lateral hypothalamus—known as hypocretins or orexins—are linked to the regulation of sleep, and recently abnormalities in the hypocretin/orexin system have been associated with narcolepsy in dogs, human beings, and mice. Rarely, narcolepsy in human patients has been reported in association with organic brain disease, such as trauma or neoplasia. In most cases of equine narcolepsy, no underlying disease can be identified, although signs have been reported in association with EPM.

Diagnosis of equine narcolepsy depends primarily on the history, clinical signs, and exclusion of other problems. Affected horses are clinically normal between episodes, and routine clinicopathologic evaluation, including CSF analysis, is normal. While the intravenous administration of physostigmine salicylate (0.1 mg/kg IV) may elicit signs of narcolepsy in affected individuals, most animals have no response. Differential diagnoses for narcolepsy include other causes of collapse, such as seizures or syncope. In general, syncope is characterized by acute collapse and unlike narcolepsy is not preceded by a gradual lowering of the head and drowsiness. The increased tonic-clonic muscle activity and postictal depression typically seen with seizures are absent in narcolepsy. Occasionally conditions that prevent horses from lying down to sleep, such as pleuritis or musculoskeletal problems, may result in signs of excessive sleepiness, and such conditions should be ruled out. Affected horses should be assessed for EPM.

Many foals affected with narcolepsy become clinically normal over time. In those horses in which narcolepsy is associated with EPM, signs may improve with appropriate treatment. However, in most cases of adult-onset narcolepsy, signs persist for life. Although drug therapy is common in human patients, information on treatment of horses is limited. Administration of the tricyclic antidepressant imipramine (250-1000 mg/500 kg q12h PO or IM) may improve clinical signs, but results are inconsistent. Affected horses should not be considered completely safe to ride, even when treated.

Supplemental Readings

- Cornelisse JC, Schott HC, Lowrie CT et al: Successful treatment of intracranial abscesses in 2 horses. *J Vet Intern Med* 2001; 15:494-500.
- Hungs M, Mignot E: Hypocretin/orexin, sleep, and narcolepsy. *Bioessays* 2001; 23:397-408.
- Mayhew IG: Disorders of behavior and personality: seizures. In Mayhew IG: *Large Animal Neurology*, pp 73-125. Philadelphia, Lea & Febiger, 1989.
- Moore LA, Johnson PJ: Narcolepsy in horses. *Comp Cont Educ Pract Vet* 2000; 22:86-89.
- Snook CS, Hyman SS, Del Piero F et al: West Nile virus encephalomyelitis in eight horses. *J Am Vet Med Assoc* 2001; 15:1576-1579.
- Uhlinger C: Clinical and epidemiological features of an epizootic of equine leukoencephalomalacia. *J Am Vet Med Assoc* 1991; 198:126-128.

CHAPTER 14.9

Brainstem and Cranial Nerve Diseases

ROBERT J. MACKAY
Gainesville, Florida

The brainstem comprises the midbrain, pons, medulla, and cerebellum. The 12 pairs of cranial nerves are the following: olfactory (I), optic (II), oculomotor (III), trochlear (IV), trigeminal (V), abducens (VI), facial (VII), vestibulocochlear (VIII), glossopharyngeal (IX), vagus (X), spinal accessory (XI), and hypoglossal (XII). The brainstem and cranial nerves coordinate and control unconscious sensory, proprioceptive, and motor functions. Disorders of these structures are characterized by one to all of a set of distinctive abnormal neurologic signs.

CLINICAL SIGNS

Mental Depression

Mental alertness is maintained by the actions of the ascending reticular activating system (ARAS), a neuronal network dispersed throughout the brainstem and some subcortical areas. The ARAS functions by continuous stimulation of the entire cerebral cortex. Consequently, reduced levels of consciousness commonly characterize brainstem disease. Increasingly severe levels of depression are termed obtundation, semi-coma, and coma. Obtundation is a reduced response to mild auditory and tactile stimuli. A horse in semi-coma is unresponsive except to strong noxious stimuli, and one in coma is unresponsive to any stimulus. Remembering that *peripheral* cranial nerve damage does not by itself cause depression is important. Mental depression can also be caused by diffuse cortical disease; thus evaluation for the presence of this sign is an important step in the process of lesion localization.

Circling

Asymmetric dysfunction of the vestibular system—including the membranous labyrinth, vestibulocochlear nerve (VIII), or nuclei—may cause circling, leaning, and head tilt. If the horse has had time to compensate visually for the effects of vestibular disease, blindfolding will exacerbate these signs. Both the position and movement of the eyes often is abnormal; thus spontaneous or positional nystagmus, as well as deviation of one eye downward and the other eye upward, may be present. Peripheral vestibular disease usually is associated with horizontal nystag-

mus, whereas nystagmus caused by central disease may be oriented in any direction. In all cases of peripheral—and in most cases of central, vestibular disease—the affected horse turns and leans—and its head tilts—toward the side of the lesion. Likewise, the ventrally deviated eye is on—and the fast phase of nystagmus is away from—the side of the lesion. Circling caused by vestibular disease needs to be distinguished from that caused by cerebral disease. In the latter case, turning is not accompanied by head tilt or body lean but often is part of a compulsive desire by the horse to keep walking forward (albeit in circles). Function of the vestibular system may further be evaluated by auditory brainstem response testing.

Facial Paralysis

Lesions of the central or peripheral parts of the facial nerve (VII) on one side may cause partial or complete hemiparesis of facial muscles evident as one to all of the following: ventral deviation of the ear, drooping of the upper eyelid, and floppiness of the lips (all on the side of the lesion) and deviation of the muzzle away from the side of the lesion. In combination, these signs cause loss of facial expression on the affected side. Secondary to such paresis, the horse may drool saliva from between imperfectly sealed lips, pack feed material between the teeth and buccal mucosa (quidding), and have exposure damage to the corneal surface (keratitis sicca). The last sign may be exacerbated by dysfunction of a parasympathetic branch of cranial nerve VII, which normally serves to stimulate tear formation. The reflex motor responses to touch are lost on the affected side of the face. This is apparent as diminished or absent retraction of the commissures of the lip and nostril, blinking of the eye in response to palpebral or corneal stimuli, and flicking of the ear when touched lightly with a hemostat or similar instrument. In addition to the facial nerve, each of these reflexes involves sensory components of the trigeminal nerve (V). Reflex facial twitch (i.e., cervicofacial reflex) is also diminished when the skin of the neck is touched firmly. In the early stages of denervation (or reinnervation), affected facial muscles may be seen to fasciculate. When paralysis is longstanding, atrophy of the parotidoauricularis muscle may be evident as a deep groove just below the base of the ear. Denervation of facial muscles may further be investigated by needle electromyography (EMG).

Atrophy of the Muscles of Mastication

Central or peripheral damage to the motor division of the trigeminal nerve (V), if severe, results in obvious atrophy of the temporalis and masseter muscles. These muscles are required for chewing. Atrophy of the other major chewing muscle, the pterygoid (located on the medial surface of the mandible), is obvious only as deepening of the supraorbital fossa on the affected side. Unilateral loss of masticatory muscle activity causes the mandible to be pulled toward the unaffected side. This is most evident as misalignment of the incisors of the upper and lower jaws. Bilateral paralysis of the muscles of mastication causes the mandible to hang open and the affected horse unable to chew. Denervation of these muscles can be evaluated both by EMG and muscle biopsy.

Dysphagia

Brainstem and cranial nerve lesions commonly cause disorders of eating or swallowing. As described above, facial nerve paralysis impairs the ability of the lips and cheeks to acquire and retain food. Bilateral paralysis of the masticatory muscles interferes with the ability to chew food and may leave the horse unable to close its mouth. Unilateral (or bilateral) paralysis of the tongue after damage to the hypoglossal (XII) nerve or nucleus interferes with the transfer of food from the mouth to the point of swallow. The complex act of swallowing requires the actions of muscles innervated by cranial nerves IX (glossopharyngeal), X (vagus), and XII (hypoglossal). Injury or damage to any of these nerves on either or both sides results in coughing and nasal regurgitation of food and saliva. In some cases, foreign material is aspirated into the airways and results in signs of lower respiratory disease. Swallowing can further be evaluated by endoscopy. In specialized settings, EMG of the swallowing muscles may provide additional information.

Respiratory Stridor

Paralysis of the vocal folds may occur secondary to dysfunction of the branches or nuclei of the vagus nerve. Unilateral paralysis causes stridor only during exercise; when both sides are affected, there is inspiratory noise even at rest.

Sensory Loss

Sensation from the structures of the head is provided by the three branches of the trigeminal—namely, ophthalmic, mandibular, and maxillary. Sensory function is evaluated by the testing of the reflexes involving cranial nerves V and VII. These have been outlined under Facial Paralysis. Each of the branches of the trigeminal can be evaluated separately by variations of the palpebral reflex. Thus gentle touching of the base of the ear and lateral and medial canthuses of the eye tests the ophthalmic, mandibular, and maxillary branches, respectively. If the horse has normal cerebrocortical function, behavioral responses to tactile or noxious facial stimuli can be used to evaluate the sensory division of the trigeminal nerve. Cortical damage may impair conscious perception of stimulation of the

opposite side of the face but has no effect on brainstem reflexes.

Blindness and Abnormal Menace Response

Injury to the optic (II) nerves, chiasm, or tracts results in blindness, dilated pupils, and loss of menace and pupillary light responses. In cases in which the damage is located peripheral to the optic chiasma, blindness will be on the same side as the injury (ipsilesional), and the menace and pupillary light responses on the same side will be lost. When the injury is central to the chiasma, menace and visual loss will be contralateral to the side of the lesion. Because of extensive crossover tracts, the pupillary light response will be preserved. With damage to the oculomotor (III) nerve or nucleus (in the midbrain), the pupil on the same side will be dilated and will lack a pupillary light response. However, the consensual pupillary light response is preserved and light shone into this eye will constrict the opposite eye. Blindness and absent menace response also result from injury to the visual pathways in the thalamus, internal capsule, and visual cortex. In these settings, pupillary light responses will be normal. Surprisingly, the cerebellum also is required for menace response. In certain diffuse cerebellar cortical diseases, such as cortical abiotrophy, the menace response is absent although vision and pupillary light responses are normal. Finally, facial nerve function is required for menace response. It is important to remember that nonneurologic injuries of the eye also can result in visual impairment. Retinal and optic nerve function can be further evaluated by electroretinography performed either in the conscious horse or under general anesthesia.

Limb Ataxia and Weakness

Injury to the vestibular system, cerebellum, or proprioceptive pathways from the spinal cord results in degrees of incoordination. In the case of vestibular injury, a wide-based staggering gait develops with tight circling and leaning toward the affected side. Blindfolding results in exacerbation of these signs. Cerebellar disease causes ataxia that is most apparent during conscious initiation of movement (e.g., change of gaits, change of direction, or movement of head to acquire food). When proprioceptive tracts to and from the spinal cord are injured, there usually also is damage to upper motor neurons, thus resulting in limb weakness.

CAUSES OF BRAINSTEM DISEASE

Equine Protozoal Myeloencephalitis

Less than 5% of horses with equine protozoal myeloencephalitis (EPM; see Chapter 2.11: "Equine Protozoal Myeloencephalitis") have obvious clinical evidence of brain disease. The most common sign is limb ataxia and weakness attributable to spinal cord damage. Among those horses that do have brain disease, signs of asymmetric brainstem involvement predominate. Typically, onset of depression is acute, along with degrees of vestibular disease and facial nerve paralysis. Without treatment, these

signs usually are progressive and may become disabling or even fatal. In addition or alternatively, dysphagia, respiratory stridor, masseteric atrophy, or any other of the signs described previously may be present. Two discrete syndromes of unilateral neurogenic muscle atrophy appear to be quite characteristic of EPM—one involving the muscles of mastication and the other the tongue. Because these signs may appear in isolation, apparently are nonprogressive and are not associated with mental depression, they are presumed to reflect very specific destruction of the nuclei of cranial nerves V and XII, respectively.

Viral Encephalitis

Eastern equine encephalomyelitis (EEE) and rabies are fatal fulminant encephalomyelitides that are characterized by severe mental depression and other signs of progressive brainstem disease that can be either symmetric or asymmetric in their distribution (see Chapter 2.5: “Viral Encephalitides”). Vestibular and facial nerve abnormalities are common in horses with EEE, whereas dysphagia often is seen in rabid horses. Brainstem damage is likely responsible for the profound depression characteristic of the “dumb” form of rabies or the prolonged period of semicomatose found in horses during the terminal phase of EEE. As these diseases progress, the clinical picture may be dominated by signs referable to other parts of the CNS. For example, cortical disease may be reflected in behavioral changes such as compulsive walking, aggression, or mania, whereas limb ataxia and weakness reflect spinal cord as well as brainstem disease. Horses with either disease usually have fever at the time of presentation, and all horses with rabies and most (>90%) horses with EEE are dead within 2 weeks of initial signs. Horses with western equine, Venezuelan equine, California, Semliki Forest, Near Eastern, Ross River, or Main Drain viral encephalomyelitis; Aujeszky's disease; or louping ill can be expected to have similar signs.

Encephalitis caused by West Nile virus (and perhaps by Murray Valley virus, another member of the Japanese B antigenic group) apparently does not have the cortical involvement characteristic of the diseases already mentioned. By contrast, symmetric or asymmetric signs of brainstem and spinal cord involvement—including muzzle fasciculations (nuclei of VII), lip, muzzle (VII) and tongue (XII) weakness, mental depression, and limb ataxia/weakness—are typical. Although signs of brainstem disease occasionally have been reported in horses with equine herpesvirus 1 (EHV-1) myeloencephalopathy, such horses often are bright and alert but exhibit signs of severe caudal spinal cord disease. Behavioral changes dominate the early clinical presentation of horses with Borna disease (“sad horse disease”), but as this generally incurable disease progresses brainstem and cranial nerves become involved.

Head Trauma

A blow anywhere to the head can cause brain damage; however, the most common cause of brainstem/cranial nerve injury is trauma to the poll. This typically occurs in horses that have reared and flipped over backwards, es-

pecially onto a hard surface. When the poll strikes the ground, impact forces are transmitted through the calvarium to the brainstem and cranial nerves. Particularly susceptible is the middle/inner ear, which may be damaged by fracture or other injury to the petrous temporal bone, thus resulting in dysfunction of the vestibular apparatus and/or damage to the facial nerve as it passes through the facial canal. Surprisingly, this type of injury most often is unilateral.

Because of sudden extension of the head as the poll hits the ground, the powerful flexor muscles of the head (rectus capitis ventralis major, longus capitis) pull violently on the basilar bones under the brainstem, thereby causing hemorrhage between or into the guttural pouches and/or fracture of the basilar bones. The latter injury directly damages the brainstem, usually causing severe mental depression and other signs of brainstem damage. This condition often is fatal. Occasionally, sub-basilar hemorrhage is so profuse that the upper airway is compromised, and life-threatening inspiratory dyspnea occurs. Poll injuries also may cause stretching of one or both optic nerves. This occurs because of the sudden backward movement of the brain when the poll strikes the ground. Resultant tearing of optic nerve fibers may result in immediate and irreversible blindness in one or both eyes. After approximately 2 weeks signs of optic nerve atrophy—including loss of vascularity and color change in the optic disk—will be obvious. If one eye is blind, the rate of and the extent to which visual compensation for vestibular dysfunction can occur is limited. The facial nerve may be injured peripherally after it emerges from the skull. When concussive damage occurs, facial nerve function is lost for days to weeks as neuropraxia and demyelination occur; however, if there is tearing of fibers within the nerve sheath, facial nerve function only recovers if reinnervation occurs successfully. Nerve fibers regrow approximately 1 cm weekly.

Temporohyoid Osteoarthropathy

The signs of temporohyoid osteoarthropathy (THO) are very similar to those of poll trauma with peripheral vestibular and facial nerve injury. Exuberant bony proliferation around the arthritic temporohyoid joint may directly impinge upon and crush the vestibular apparatus. Perhaps more commonly, sudden movements of the tongue or larynx transmitted via the stylohyoid bone and fused temporohyoid (TH) joint may exert sufficient pressure on the petrous temporal bone to fracture it and damage the facial nerve or vestibular structures. In rare instances, bacterial otitis media may subsequently extend centrally through a fracture defect to cause epidural abscess or meningitis.

Lightning Strike

Clinical signs ranging from sudden death to mild ataxia may be caused by lightning strike. Commonly, electrical current flows centrally via the ear canal and causes peripheral and sometimes central vestibular disease. Single lines may be visible in the hair coat, or evidence of lightning strike may be seen on nearby trees or other animals.

Tumor

Virtually any sign of brainstem dysfunction may be caused by epidural neoplasms that expand within the confines of the caudal fossa of the skull. The specific signs seen depend upon the part of the brainstem and/or cranial nerves affected. Despite some fluctuations over time, clinical signs caused by expanding tumors are expected to get worse over time, usually over days to weeks after the first onset of clinical signs. Malignant melanoma in gray horses appears to be predisposed to the brainstem. Less commonly, lymphoma may behave in similar fashion. Rarely, pituitary adenoma may expand sufficiently to cause blindness consequent to pressure injury to one or both optic nerves.

Botulism and Tetanus

Flaccid paralysis (botulism) or spasm (tetanus) of the muscles innervated by cranial nerves results from the actions of potent clostridial exotoxins acting at the neuromuscular junction or inhibitory interneurons, respectively. Paralysis or spasm of the muscles that are involved in swallowing, breathing, facial expression, and mastication occurs. Although these effects are life-threatening, brainstem function is otherwise not affected.

Polyneuritis Equi

Immune-mediated attack against the cranial nerve roots may be evident as asymmetric cranial nerve dysfunction. Facial paralysis may be the most common presentation. This syndrome more typically presents as cauda equina syndrome that results from destruction of the caudal nerve roots (neuritis of the cauda equina, see Chapter 14.6: "Bladder, Rectal, Anal, and Tail Paralysis; Perineal Hypalgesia; and Other Signs of Cauda Equina Syndrome").

Toxicity

The most common brainstem-associated toxicities are the vestibulocerebellar syndromes that are suspected to be caused by tremorgenic mycotoxins. These mycotoxins are based on lysergic acid and include that produced by perennial ryegrass, *Paspalum* spp. (dallis grass, Bahia grass), and Bermuda grass. The signs are caused by imbalance of centrally acting excitatory and inhibitory neurotransmitters. Ataxia of the limb and trunk occurs without weakness, as do tremor and fasciculation of cutaneous and anti-gravity muscles. Even at rest when standing or in sternal recumbency, affected horses rock and sway side-to-side and backwards-forwards. Despite these signs, affected horses usually are bright and alert and eat normally. Signs are exacerbated by handling, and in severe cases, horses may fall to the ground in convulsions. Signs resolve completely over days to weeks after horses are removed from affected pasture or hay. Similar but irreversible signs result from the actions of bacteria that infect nematode-damaged seedheads of annual ryegrass or blown grass. Rarely, horses with chronic lead poisoning, Australian stringhalt (found in horses grazing Catsear or dandelion), or delayed organophosphate toxicity will have degrees of laryngeal dysfunction because of degeneration of the vagus nerve or its branches.

Bacterial Meningoencephalitis

Hematogenous or direct bacterial seeding of the meninges around the brainstem may occur. Meningitis is particularly likely in bacteremic neonates but may occur at any age. Profound mental depression and high fever are the most consistent signs of meningitis around the brainstem. Abscesses may form in the epidural spaces of the brainstem or in the basilar veins, where blood flows slowly. These abscesses cause pressure injury of the adjacent brain and behave much like the epidural tumors described previously. *Borrelia burgdorferi* (Lyme disease, see Chapter 2.7: "Lyme Disease") and *Listeria monocytogenes* are examples of specific bacteria that occasionally may cause brainstem encephalitis in horses.

Guttural Pouch Diseases

Cranial nerves IX, X, XI, and XII are contained in mucosal folds on the caudodorsal aspect of the medial compartment of the guttural pouches. The mucosa at this site is subject to mycotic infection (guttural pouch mycosis; see Chapter 7.7: "Guttural Pouch Disease") that causes signs of cranial nerve dysfunction, usually unilaterally. The internal carotid artery and cranial cervical sympathetic ganglion share these mucosal folds, and additional clinical signs (epistaxis and Horner's syndrome, respectively) reflect involvement of these structures. Similar neurologic signs may accompany abscessation of the retropharyngeal lymph nodes, guttural pouch empyema, chondroid impaction, and chemical scalding of the guttural pouch mucosa.

Cerebellar Abiotrophy

The cerebellum of certain lines of Arabian horses and Götland Pony foals undergoes premature degeneration shortly before or after birth. These foals have jerky, dysmetric movements and intention tremor. Although they can see normally, affected foals have no menace response. Signs are initially progressive for weeks or months and then often level out.

Parasitic Encephalitis

Aberrant parasite migration is a rare cause of brainstem disease. Signs depend upon the migratory path of the parasite. In most cases, a single parasite is involved: *Strongylus vulgaris*, *Setaria digitata*, *Draschia megastoma*, and *Hypoderma* spp. all have been found in this setting. The opportunistic rhabditid nematode *Halicephalobus gingivalis* (previously known as *Miconema deletrix* and *Halicephalobus deletrix*) may invade the brainstem in enormous numbers, thus causing signs similar to viral encephalitis. In addition, the parasite may invade soft tissues elsewhere in the body and cause nasal, oral, or renal granulomatous masses.

Hypoxic-Ischemic Encephalomyelopathy

The predominant cortical signs of hypoxic-ischemic encephalomyelopathy (HIE) are described in Chapter 12.4. In some foals, severe depression reflects brainstem damage. Specific asymmetric signs of ischemic damage to brainstem nuclei may be present. For example, some foals

have signs of vestibular diseases such as head tilt and circling. These signs improve slowly and incompletely.

DIAGNOSIS

The diseases described previously can seldom be diagnosed conclusively by use of a single test. In most cases, the diagnostician must analyze signalment; clinical signs; results of blood and CSF tests; and imaging, endoscopic, or electrodiagnostic examinations.

Signalment

Although it seldom clinches a diagnosis, proper consideration of breed, location, age, and vaccination history can considerably narrow the range of possibilities. For example, cerebellar abiotrophy is mainly recognized in Arabian and Götland Pony breeds. EPM is very rare in ponies and zebras, whereas Quarter Horses are perhaps more likely to suffer from THO than are horses of other breeds. EPM also is found almost exclusively in horses that have spent time in the Americas, whereas West Nile encephalomyelitis (WNE) should be suspected in areas currently experiencing epizootics (e.g., in 2001, Israel, parts of Europe, and eastern and southeastern United States). EEE and botulism are high on the list of differential diagnoses in Florida and Kentucky, respectively—states where these diseases are enzootic—and Borna disease occurs sporadically throughout Germany. Tremorgenic mycotoxicoses obviously are limited to areas with the appropriate forages and environmental conditions. For example, perennial ryegrass staggers should be considered in horses with the appropriate signs in the northwestern United States, Australasia, South Africa, and parts of Europe; Bermuda hay (or grass) staggers apparently is most likely in Florida; and Australian stringhalt occurs in Australasia, South Africa, and the western United States. Bacterial meningitis, ischemic CNS injury, and cerebellar abiotrophy are much more likely in neonates than in older foals and adults, whereas THO and tumors are expected only in middle-aged or older horses. Reliable vaccination history obviously is important in ranking the likelihood of specific diseases. Proper interpretation of vaccination history requires knowledge of vaccine efficacy. For example, an initial series of inoculations with tetanus or *Clostridium botulinum* type-B toxoid may protect horses for several years. In contrast, killed vaccines against EEE, WEE, VEE, or WNE likely are not protective until 2 weeks after the initial series and probably are effective for no longer than 6 months. The efficacy of the commercial EPM vaccine is still unknown; therefore history of its use should not influence diagnostic considerations.

Clinical Signs

Abnormal neurologic signs can be used to pinpoint the site of a lesion or lesions. Of particular importance is the distinction between peripheral and central lesions (as discussed above). For example, signs of peripheral vestibular disease could not be ascribed to EPM but would be compatible with THO or poll trauma. Signs consistent with multifocal dis-

ease tend to implicate EPM as the cause. For example, unilateral wasting of masticatory muscles along with atrophy of gluteal muscles are classic signs of this disease. Nonneurologic clinical signs also can be useful; horses with viral or bacterial diseases often are febrile, but traumatic, toxic, or protozoal diseases typically do not cause fever.

Blood Tests

Results of routine hematologic and chemical analyses are not usually particularly helpful in discriminating among neurologic diseases. In general, there likely will be nonspecific inflammatory changes (leukocytosis, left shift, hyperfibrinogenemia) in horses with bacterial diseases and lymphopenia in horses with EEE or other viral acute encephalitides. Serologic tests designed to detect antibodies against encephalitis agents are variably useful. Hemagglutination inhibiting and neutralizing antibody titers against the agents of EEE and WNE are usually high in horses with these diseases, but they also can be induced by vaccination.

For both EEE and WNE, IgM-capture ELISAs have been developed and appear to be able to distinguish disease from vaccinal titers. High titers against EHV-1 or *Borna virus*, and positive Western blots for *Sarcocystis neurona* antibody are highly sensitive for diagnosis of EHV-1 myeloencephalopathy, Borna disease, and EPM, respectively, but because infection with the causative agents usually is subclinical, these tests have very low specificity. Vaccination also can cause seroconversion against EHV-1 and *S. neurona*. Detection of circulating botulinum toxin would confirm a diagnosis of botulism, but toxin is only rarely found in clinical cases. Assays are available in research laboratories for anti-P2 myelin antibody; however, it is now apparent that this test is insufficiently specific for diagnosis of polyneuritis equi.

Cerebrospinal Fluid Analysis

Analysis of cerebrospinal fluid (CSF) is an invaluable diagnostic aid. Very high nucleated cell counts ($>500/\mu\text{l}$) are characteristic of bacterial infection, whereas counts of $10\text{--}500/\mu\text{l}$ are more consistent with viral, parasitic, immune-mediated, and certain bacterial diseases (e.g., neuroborreliosis, listeric encephalitis). Most bacterial diseases are characterized by neutrophilic cellular effusion. CSF from horses with viral brain diseases more typically have mononuclear pleocytosis; however, in acute severe EEE and WNE, up to 25% neutrophils may be present. Eosinophils are expected in parasitic diseases, but some cases have a predominantly mononuclear or neutrophilic response. CSF from horses with EPM usually has normal cell count ($<7\text{ cells}/\mu\text{l}$) but a minority of cases have a mixed cell response and $10\text{--}100\text{ cells}/\mu\text{l}$ of CSF. The protein concentration of CSF always increases with elevated cell count. In EHV-1 myeloencephalopathy and in some cases of EPM, increased protein concentration with normal cell count (albuminocytologic disassociation) occurs. CSF also can be analyzed for *S. neurona* antibodies by Western blot. This test has much higher specificity for diagnosis of EPM than does Western blot of blood. Immediately after trauma, large numbers of erythrocytes in CSF

may be present. This changes to yellow discoloration (xanthochromia) as hemoglobin is processed to bilirubin. Xanthochromia also is found in CSF of horses with EHV-1 myeloencephalopathy.

Endoscopy

Examination of the upper respiratory tract provides important information about pharyngeal and laryngeal motor and sensory function. Inspection of the interior of the guttural pouches allows diagnosis of mycosis, empyema, or THO (evident by thickening and discoloration of the stylohyoid bone and TH joint).

Diagnostic Imaging

Conventional radiography is essential for diagnosis of skull fractures, middle/inner ear injury, and THO. Middle or inner ear injury is usually evident as sclerosis of the affected osseous bulla. THO is best appreciated as thickening of the affected bone and ossification of the osseous bulla on a dorsoventral view taken in the standing horse or a ventrodorsal view taken in the recumbent animal. These conditions and any associated fractures can be assessed with greater precision by computed tomography (CT). In addition, CT and magnetic resonance imaging may be the only way to diagnose *ante mortem* soft-tissue changes such as tumors and abscesses.

Electrodiagnostics

Needle electromyography can be used to detect denervation (>10 days after injury) in facial and masticatory muscles. Auditory brainstem response testing (also known as brainstem auditory evoked response) allows localization of the lesion in vestibular disorders. These procedures are available at many referral centers.

TREATMENT

Antiinflammatory Drugs

In horses that have mental depression or other signs of brainstem dysfunction after poll or other head trauma, high-dose corticosteroid therapy probably is beneficial. One protocol (adapted from human neurology) is methylprednisolone sodium succinate (30 mg/kg IV, then 5-10 mg/kg q6h for 24 hours). This treatment should be started within several hours of the time of injury. Alternatively, dexamethasone (0.05-0.1 mg/kg IV or 0.1-0.2 mg/kg PO q12h for 1-3 days) has potent antiinflammatory effect in horses with traumatic or infectious injury. Dexamethasone treatment appears to be especially useful in horses with subacute mild EEE and EHV-1 myeloencephalopathy but also can be used in conjunction with antimicrobials or anthelmintics during the early stages of EPM or verminous encephalitis. To provide important additional antiediator, antipyretic, and analgesic effect, a cyclooxygenase inhibitor (e.g., 1.1 mg/kg flunixin meglumine IV or IM q12-24h) should be given to all horses with acute onset of brainstem or peripheral cranial nerve dysfunction.

Antioxidant Treatments

The cell membranes of injured neurons are subject to oxidant damage; therefore antioxidant therapy is logical—even if largely unproved—in brainstem injury. Typical regimens are dimethyl sulfoxide (DMSO; 1 g/kg as a 10% solution, q12h, IV or intragastric, for 5 treatments), vitamin E (20 IU/kg q24h, IV, SQ, or PO), or mannitol (0.5-2 g/kg, IV q6h as a 20% solution).

Fluid and Electrolyte Therapy

Ensuring full hydration is important to maximizing perfusion of the brain. Previous notions about the value of intentional dehydration in brain injury probably are incorrect. Because extracellular calcium may contribute to neuronal cell death, fluids should be calcium-free whenever possible. In contrast, magnesium may inhibit the actions of the toxic excitatory amino acids that contribute to neuronal necrosis in the damaged brain. For this purpose, MgSO₄ may be added to fluids at the rate of 1-2 g/L. MgSO₄ also can be given IV for control of the muscle spasms of tetanus (given to effect until the patellar reflex barely remains) or for the tremors of staggers syndromes (20 g in 5 L fluids given IV as necessary to an adult horse).

Antimicrobials and Anthelmintics

Antiprotozoal therapy for EPM is described in Chapter 2.11. Prolonged broad-spectrum IV antibiotics are needed for the treatment of bacterial meningitis or other bacterial intracranial disease. More specific treatments can be selected as results of bacterial culture and sensitivity testing become available. Protocols for antibiotic treatment of neonatal bacterial sepsis are described in Chapters 1.1 and 12.6. Even with excellent antimicrobial therapy, mortality rates exceed 80% in foals with meningitis. To prevent extension of infection centrally around the brain, antibiotics (trimethoprim-sulfonamide, 30 mg/kg q12h) also should be given in any case of open skull fracture (i.e., fracture associated with skin wound, sinus injury, or leakage of CSF from an external ear) or THO. When parasitic encephalitis is suspected, high-dose fenbendazole (10 mg/kg q24h for 5 days or 50 mg/kg for 2 successive days) is an economic and effective treatment. Ivermectin or moxidectin also are effective systemically; however, their rate of parasite kill may be slower than that of fenbendazole.

Surgery

Skull fractures of the frontal, zygomatic, and parietal bones may be stabilized by surgical procedures that are discussed in standard surgical texts. Fractures or separations of the petrous temporal or basilar bones likely cannot be repaired and must be managed by minimizing physical stresses on involved bones. Midbody stylohyoidectomy now is performed commonly to minimize the stresses on an arthritic, ankylosed TH joint in horses that already show neurologic signs of THO. Preliminary evidence suggests that this procedure should not be performed bilaterally even if signs are bilateral.

Supplemental Readings

Blythe LL: Otitis media and interna and temporohyoid osteoarthropathy. *Vet Clin North Am Equine Pract* 1997; 13:21-42.

Cheeke PR: Endogenous toxins and mycotoxins in forage grasses and their effects on livestock. *J Anim Sci* 1995; 73:909-918.

Greet TR: Outcome of treatment in 35 cases of guttural pouch mycosis. *Equine Vet J* 1987; 19:483-487.

Kinde H, Mathews M, Ash L et al: *Halicephalobus gingivalis* (H. deletrix) infection in two horses in southern California. *J Vet Diagn Invest* 2000; 12:162-165.

Martin L, Kaswan R, Chapman W: Four cases of traumatic optic nerve blindness in the horse. *Equine Vet J* 1986; 18:133-137.

SECTION XV

Toxicology

Edited by Dr. Mike Murphy

CHAPTER 15.1

Introduction to the Toxicology Section

MIKE K. MURPHY
Saint Paul, Minnesota

Equine toxicology, or the study of adverse effects of chemical agents in the horse, has been discussed in detail in previous editions of this text. (Topics discussed in previous editions are identified by edition in Table 15.1-1.) This edition focuses on feed-related toxicoses.

The scope and depth of each chapter in this section aims to supply information that the equine practitioner needs to know. Feed-associated toxicoses in horses may be categorized as those that occur on pasture, those that occur in hay, and those that occur in finished feeds. These toxins may also be categorized by source (e.g., plants, insects, and fungi). Both categorization schemes are used in this section.

Pasture, hay, and feed are discussed in this section as the most common sources of toxins to which horses are exposed. Nigropallidal encephalomalacia is a plant-induced toxicosis that primarily occurs on pasture. Plant-induced equine mycotoxicoses also generally occur on pasture, although some of the plants are rarely baled in hay. Blister beetle toxicosis is also a primary concern in hay. Hoary alyssum, pyrrolizidine alkaloid poisoning, and clover-associated photosensitization may occur on pasture or in hay.

Molds from pasture, hay, or feed sources may cause disease in horses. The horse owner does not always appreciate the distinction between mycoses, mold allergies, and mycotoxicoses in horses, so a very superficial overview of these conditions is included here. The ergopeptide alkaloids are induced by endophytes in the case of tall fescue toxicosis and external molds in the case of ergotism. These different sources have lead to descriptions of syndromes with various names that appear to be explained by the same or very similar chemicals in the final analysis. Mycotoxins are quite often formed in grains while still in the field, so mold counts or identifications are rarely of value in identification of these toxicoses. Direct testing of the chemical mycotoxin is necessary, as with aflatoxin.

Trace mineral supplementation is now commonplace in equine husbandry. Excessive supplementation and feed mixing errors have led to toxicoses in horses as in other livestock. An interesting example of this phenomenon is selenium, of which supplementation or parenteral dosing is the source of toxicosis for much of the country, but pasture is a primary source for the Western United States.

Table 15.1-1

Current Therapy in Equine Medicine Index of Topics by Edition

	4th Edition	3rd Edition	2nd Edition	1st Edition
Blister beetle toxicosis				p 588
Carbon tetrachloride			p 665	p 590
Diagnostic toxicology	p 652	p 337		
Drugs of abuse in horses			p 689	
Feed-associated poisonings	p 665	p 366		

Continued

Table 15.1-1

Current Therapy in Equine Medicine Index of Topics by Edition—cont'd

	4th Edition	3rd Edition	2nd Edition	1st Edition
Fescue toxicosis	p 670			
Forensic necropsy of the horse	p 655			
Heavy metal toxicoses		p 344		p 592
Industrial toxicants		p 363	p 667	
Insecticides		p 358		
Leukoencephalomalacia/ stachybotryotoxicosis		p 377	p 656	p 580
Management of toxicoses		p 346	p 653	p 577
Medicolegal investigations	p 657			
Mycotoxins	p 668			
Petroleum products			p 666	p 591
Phenothiazine			p 665	p 590
Rodenticides			p 660	p 584
Selenium			p 670	p 593
Snake bite			p 663	p 587
Sudden unexplained death		p 340	p 685	p 611
Toxic plants	p 649	p 372	p 672	p 595
Toxicity of pharmacologic agents		p 353		
Water quality			p 682	p 607

CHAPTER 15.2

Nigropallidal Encephalomalacia

PATRICIA TALCOTT

Moscow, Idaho

Nigropallidal encephalomalacia is a disease only described in horses. Although donkeys and mules may be susceptible as well, no clinical reports exist that describe this disease in these animals.

CAUSATIVE AGENTS

Two plants in the Asteraceae family are capable of causing this disease—yellow star thistle (*Centaurea solstitialis*) and Russian knapweed (*Acroptilon repens*). *Centaurea melitensis* (Malta star-thistle), a native of central Texas, may also cause disease, but no published cases have been reported to date. Yellow star thistle is an annual weed of 1 to 6 ft with a single, erect, woody, rigid stem. The basal pinnate leaves become linear as they progress up the stem. The stem and leaves are covered with fine, cottony hairs. In the spring each branch has an ovoid, spiny base surrounding a cluster of bright yellow florets. Yellow star this-

tle is an aggressive, noxious, allelopathic weed that can heavily infest rangeland and abandoned crop land. This plant is most commonly found in California, Oregon, and Idaho, but is found scattered in local spots elsewhere in the United States.

Russian knapweed is a perennial that forms dense colonies with deep, widely spreading rhizomes. The stems are erect and 1 to 3 ft tall. The lower leaves are deeply indented and 2 to 4 in long, and the upper leaves tend to be narrow and entire. The solitary cone-shaped flowery heads are pink-purple to blue-white. The involucre bracts form with rounded papery margins. Russian knapweed has a much broader distribution throughout the intermountain states.

Many people have investigated the potential toxic principle(s) of these two plants. Current research suggests that the compound DDMP (2,3-dihydro-3,5-dihydroxy-6-methyl-4[H]-pyran-4-one) plays a critical role in the de-

Table 15.1-1

Current Therapy in Equine Medicine Index of Topics by Edition—cont'd

	4th Edition	3rd Edition	2nd Edition	1st Edition
Fescue toxicosis	p 670			
Forensic necropsy of the horse	p 655			
Heavy metal toxicoses		p 344		p 592
Industrial toxicants		p 363	p 667	
Insecticides		p 358		
Leukoencephalomalacia/ stachybotryotoxicosis		p 377	p 656	p 580
Management of toxicoses		p 346	p 653	p 577
Medicolegal investigations	p 657			
Mycotoxins	p 668			
Petroleum products			p 666	p 591
Phenothiazine			p 665	p 590
Rodenticides			p 660	p 584
Selenium			p 670	p 593
Snake bite			p 663	p 587
Sudden unexplained death		p 340	p 685	p 611
Toxic plants	p 649	p 372	p 672	p 595
Toxicity of pharmacologic agents		p 353		
Water quality			p 682	p 607

CHAPTER 15.2

Nigropallidal Encephalomalacia

PATRICIA TALCOTT
Moscow, Idaho

Nigropallidal encephalomalacia is a disease only described in horses. Although donkeys and mules may be susceptible as well, no clinical reports exist that describe this disease in these animals.

CAUSATIVE AGENTS

Two plants in the Asteraceae family are capable of causing this disease—yellow star thistle (*Centaurea solstitialis*) and Russian knapweed (*Acroptilon repens*). *Centaurea melitensis* (Malta star-thistle), a native of central Texas, may also cause disease, but no published cases have been reported to date. Yellow star thistle is an annual weed of 1 to 6 ft with a single, erect, woody, rigid stem. The basal pinnate leaves become linear as they progress up the stem. The stem and leaves are covered with fine, cottony hairs. In the spring each branch has an ovoid, spiny base surrounding a cluster of bright yellow florets. Yellow star this-

tle is an aggressive, noxious, allelopathic weed that can heavily infest rangeland and abandoned crop land. This plant is most commonly found in California, Oregon, and Idaho, but is found scattered in local spots elsewhere in the United States.

Russian knapweed is a perennial that forms dense colonies with deep, widely spreading rhizomes. The stems are erect and 1 to 3 ft tall. The lower leaves are deeply indented and 2 to 4 in long, and the upper leaves tend to be narrow and entire. The solitary cone-shaped flowery heads are pink-purple to blue-white. The involucre bracts form with rounded papery margins. Russian knapweed has a much broader distribution throughout the intermountain states.

Many people have investigated the potential toxic principle(s) of these two plants. Current research suggests that the compound DDMP (2,3-dihydro-3,5-dihydroxy-6-methyl-4[H]-pyran-4-one) plays a critical role in the de-

velopment of this disease. This compound has been shown to be highly reactive, and shows selective and specific binding to the dopamine transporter in equine brain tissue. The compound has also been shown to be cytotoxic to selective regions of the brain *in vitro*.

TOXIC DOSE

Toxicity in horses is the result of substantial continuous ingestion of plant material (85%-200% of their body weight) during a period of several weeks to months. Most poisonings occur in the spring and summer when horses consume the young, fresh, green plant in a pasture setting. The plant is also considered to be toxic when dried, so hay contamination is also a possible route of exposure. Neither of the two plants mentioned previously is considered palatable at any stage of growth, nor are they readily grazed when they become mature (the plant is more woody and spiny, in the case of yellow star thistle). Some animals appear to become addicted to the plants and will preferentially seek them out even when other more palatable forages are available.

CLINICAL SIGNS

In this author's experience, young horses (usually younger than 3 years) are most commonly affected with nigropallidal encephalomalacia, although horses as old as 18 years have been affected. No progression of signs appears to occur and the onset is typically quite acute in nature. The most commonly reported signs include a unique inability to drink water or swallow food—an inability to hold, masticate, and move the bolus of food to the back of the pharynx. Affected horses are often found extremely depressed, standing with their heads drooped down and engaged in continuous chewing with food material slowly dropping from their mouths. Edema of the head area is common. Other signs seen are yawning, ataxia, muscle tremors, aimless wandering, hypermetria,

involuntary lip twitching, and hypertonicity of the lips and tongue. Death, if it occurs naturally, is usually considered a result of starvation.

PATHOLOGIC LESIONS

Bilateral (rarely unilateral), symmetric, nonprogressive focal necrosis and malacia of the globus pallidus and/or substantia nigra are characteristic lesions of this disease. Other portions of the brain can be less severely affected, particularly in horses exposed to Russian knapweed. No specific abnormalities are noted on a complete blood count and serum chemistry panel, and there seems to be no way to predict the onset of this disease. Diagnosis is most commonly confirmed by postmortem examination of brain tissue. Magnetic resonance imaging of the brain has been used to confirm the existence of the lesions antemortem, however.

TREATMENT AND PROGNOSIS

No specific treatment exists for this disease other than good nursing care. This care may include multiple, daily intubations with water and good-quality forage, in addition to vitamin supplementation. In this author's experience, complete recovery is not possible.

Supplemental Readings

- Burrows GE, Tyrl RJ: *Centaurea*. In Burrows GE, Tyrl RJ (eds): *Toxic Plants of North America*, p 156, Ames, Iowa, Iowa State University Press, 2001.
- Sanders SG, Tucker RL, Bagley RS et al: Magnetic resonance imaging features of equine nigropallidal encephalomalacia. *Vet Radiol Ultrasound* 2000; 42:291-296.
- Young S, Brown WW, Klinger B: Nigropallidal encephalomalacia in horses fed Russian knapweed (*Centaurea repens* L.). *Am J Vet Res* 1970; 31(8):1939.

CHAPTER 15.3

Plant-Induced Cardiac or Skeletal Muscle Necrosis

BRYAN STEGELMEIER

Logan, Utah

Cardiac and skeletal muscles are specialized tissues with high nutrient requirements and extensive networks of excitable membranes; thus they are uniquely susceptible to many natural toxins. Although poisoning by cardiotoxic and myotoxic plants is infrequent, the effects of poisoning are probably more extensive than is outwardly apparent. In common poisoning scenarios animals eat or are fed lethal doses of plants or contaminated feeds that result in epidemic-like crippling or death of the exposed animals. However, inapparent or subclinical poisonings probably occur much more frequently and damage many more animals. Many subclinical poisonings do not produce clinical signs but result in loss of function or scarring that prevents animals from developing to their full genetic potential. This effect is especially true in horses, in which performance is measured by athletic ability and cardiovascular stamina.

Plant myotoxins may be transferred to growing fetuses and neonates during gestation or lactation. In addition, fetal and neonatal animals are often more susceptible to certain myotoxins. Some lipid-soluble toxins are preferentially excreted in milk; this excretion results in neonatal poisoning without apparent maternal toxicity. The resulting cardiac or skeletal muscle scarring may not produce clinically apparent diseases, but the resulting scars may reduce the animal's performance. Such scarring supports the old saying that performance-challenged animals "lack heart." Additional research is needed to better define the effects of subclinical poisoning, neonatal and fetal susceptibility, and the prognosis for animals that have been previously poisoned. This chapter briefly reviews the cardiotoxic and myotoxic plants that most commonly poison horses in North America.

SENNA

Senna occidentalis (cassia, coffee weed, or coffee senna) and *Senna obtusifolia* (senna or sicklepod) are annual shrubs indigenous to the southeastern United States and Texas. Green and dry vegetative portions and the seeds of these plants are toxic. Doses of 1.5% to 2% of the horse's body weight have been shown to be toxic. The plants are most often found in the southeastern United States where both are common weeds that infest corn, sorghum, and soybeans. Senna seeds can be harvested with small grains and thus contaminate harvested foods and feeds. Neither plant is highly palatable, and poisoning is most common in No-

vember and December—when animals are more likely to consume the plant after frosts.

Although all toxins have not been identified, water-soluble anthraquinones are speculated to produce most of the cathartic and myotoxic effects. These quinones are thought to uncouple electron transfer and cause mitochondrial damage similar to adriamycin. Within several days of exposure poisoned animals develop colic, tenesmus, diarrhea (nearly all senna species are potent cathartics), and progressive muscular incapacitation seen as lethargy, weakness, stumbling, swaying gait, and muscular tremors. Fatally poisoned animals develop incoordination, recumbency, hemoglobinuria, and increases in serum aspartate aminotransferase (AST) and creatine kinase (CK) enzyme activities. Lesions characteristic of poisoning include nephrosis, pulmonary edema, centrilobular hepatic necrosis, and muscular streaking caused by pale degenerative cardiac and skeletal myocytes. Some animals may develop congestive heart failure. Treatment is primarily symptomatic to relieve gastroenteritis and colic and separation of the animal from the plant. Little information is available concerning the prognosis of previously poisoned animals.

FALSE LUPIN

Thermopsis montana (false lupin or mountain thermopsis) is a pealike plant found in the western United States. The plant is a perennial legume that grows to 0.5 m high in many mountain meadows, desert shrubs, and grassland plant communities (Figure 15.3-1). Toxicity is attributed to a combination of quinolizidine alkaloids (n-methylcytisine, cytisine, 5,6-dehydrolupanine, thermopsine, and anagryrine). Although the mechanism of action is not known, it is highly toxic; doses of 1.1 mg/kg administered for several days have been reported to be lethal in cattle. Similar sensitivity to poisoning has been found in clinical poisonings in horses, but the toxic dose has not been verified experimentally. Acute poisoning in children from the ingestion of as few as 6 seeds has been reported. Signs of poisoning begin within 3 days of exposure and include colic, depression, anorexia, weakness, trembling, recumbency, and death with increased serum AST, lactate dehydrogenase (LDH) and CK enzyme activities. Lesions include pale streaking of skeletal muscle caused by muscle degeneration and necrosis. Treatment may include administration of charcoal in acute poisoning with supportive care to sustain recumbent animals.



Figure 15.3-1 *Thermopsis montana* (also known as false lupin or mountain thermopsis).

WHITE SNAKEROOT AND RAYLESS GOLDENROD

These two plants are discussed together because they have the same toxin and produce similar toxicity. *Eupatorium rugosum* (white snakeroot) is located in many of the wooded areas of central and eastern United States (Figure 15.3-2). *Haplopappus* or *Aplopappus* spp. (rayless goldenrod, jimmyweed, burrow weed) is a shrub found in the southwestern United States. Both are toxic to all animals and their toxicity in humans has been known as *milk sickness*. Toxicity has been attributed to tremetol, a mixture of fat-soluble, high-molecular-weight alcohols that fractionates into tremetone, dihydrotremetone, and hydroxytremetone (ketones). Green, dry, and frosted plants remain toxic, but poisoning usually occurs after frosts when the plants remain succulent and green. The toxin is preferentially excreted in milk (lipid soluble) resulting in "relay toxicity" that affects the nursing neonate often without maternal toxicity. Pasteurization does not alter toxicity and the effects of toxicity are cumulative. As lactating animals are seemingly protected, toxicity varies between 1% and 10% body weight. Poisoned horses develop trembles, dyspnea, slobbering, swallowing difficulties, unsteady gait, and patchy sweating. Cardiac changes include arrhythmias, jugular distention and pulse, stocking up and ventral edema, and increased AST, LDH, and CK serum enzyme activities. Gross and histologic changes include necrosis, fibrosis, and congestive heart failure with myocardial degeneration. Treatment is symptomatic with oral activated charcoal to reduce absorption of the toxins.

CARDIAC GLYCOSIDE-CONTAINING PLANTS

Cardiac glycoside-containing plants are highly toxic and poisoning in horses has been reported. The toxins from these plants have digitalis-like action and they are highly toxic with median lethal doses of between 100 and 200 mg/kg for most domestic animals. These toxins interfere with the Na/K pump resulting in decreased intracellular K and a decreased resting membrane potential. High doses



Figure 15.3-2 *Eupatorium rugosum* (also known as white snakeroot).

result in asystole, progressive interference with cardiac electric conduction, and increased vagal tone to the sinoatrial (SA) and atrioventricular (AV) nodes. The signs of toxicity include colic, asystole, sweating, diarrhea, anorexia, vomiting, bradycardia, alterations in heart rate, cold extremities, dilation of pupils, cardiac arrhythmias, discoloration of mucous membranes, and death. The few lesions present include minimal myocardial hemorrhage, minimal myofiber vacuolation, and minimal inflammatory myocardial infiltrates. In most cases all parts of the plant are toxic and toxicity persists in dried or stored plants.

Important species of plants likely to cause problems in North America include *Digitalis purpurea* (foxglove), a biennial European herb that is common on the West Coast; *Nerium oleander* (oleander), an ornamental evergreen shrub used throughout North America; *Convallaria majalis* (lily of the valley), an ornamental plant found throughout North America; *C. montana* (lily of the valley), which is native in mountainous areas of the eastern United States; *Apocynum* spp. (dogbane, Indiana hemp), a perennial erect plant found throughout North America; *Rhododendron* spp., a deciduous shrub and ornamental used throughout North America; and *Asclepias* spp. (milkweeds) erect perennial herbs found in moist areas throughout North America and much of the world. Less common plants include *Adonis aestivalis* (pheasant eye), *Kalmia* spp. (laurels), and *Thevetia peruviana* (yellow oleander). Treatment is similar to that of digitoxin poisoning and ranges from supportive treatment of the congestive heart failure and oral dosing with activated charcoal to reduce absorption to more expensive intravenous treatment with specific digitalis antiserum (Digibind).

OTHER PLANTS

This chapter is limited and excludes many myotoxic plants. Other plants such as *Karwinskia humboldtiana*

(coyotillo, buckthorn), *Vicia villosa* (hairy vetch), *Cestrum diurnum* (day-blooming jessamine), or several others may cause significant local problems. Local extension agents, herbaria, and recent texts in the supplemental reading section are an invaluable aid to identify these plants, understand their toxicity, and prevent poisoning.

Supplemental Readings

Baker DC, Keeler RF: *Thermopsis montana*-induced myopathy in calves. J Am Vet Med Assoc 1989; 194:1269-1272.
Burrows GE, Tyrl RJ: Toxic Plants of North America, Ames, Iowa, Iowa State University Press, 2001.

Galey FD, Holstege DM, Plumlee KH et al: Diagnosis of oleander poisoning in livestock. J Vet Diagn Invest 1996; 8:358-364.
Irigoyen LF, Graca DL, Barros CSL: Experimental poisoning by *Cassia occidentalis* in horses. Pesquisa Veterinaria Brasileira (Braz J Vet Res) 1991; 11:35-44.
Kingsbury JM: Poisonous Plants of the United States and Canada, Englewood Cliffs, NY, Prentice-Hall, 1964.
Knight AP, Walter RG: A Guide to Plant Poisoning of Animals in North America, Jackson, Wyo, Teton Newmedia, 2001.
Martin BW, Terry MK, Bridges CH et al: Toxicity of *Cassia occidentalis* in the horse. Vet Hum Toxicol 1998; 23:416-417.
Spoerke DG, Murphy MM, Wruk KM et al: Five cases of *Thermopsis* poisoning. J Toxicol Clin Toxicol 1988; 26:397-406.
Thompson LJ: Depression and choke in a horse: probable white snakeroot toxicosis. Vet Hum Toxicol 1989; 31:321-322.

CHAPTER 15.4

Blister Beetle Toxicosis

STAN W. CASTEEL
TIM J. EVANS
Columbia, Missouri

Blister beetle poisoning is a cantharidin intoxication of livestock such as horses, cattle, goats, and sheep. Primarily a problem in horses, it induces severe and often fatal colic. Ruminants are less commonly affected, although they are similarly sensitive. Cantharidin poisoning also has been reported in chickens, emus, and humans. Technologic change in the way forage is harvested occurred in the 1960s and resulted in the emergence of blister beetle poisoning in livestock. The cutting and crimping of forage by a single harvesting implement (i.e., a windrower) kills and traps the beetles in hay for baling. Because these beetles swarm for mating purposes, dozens may be incorporated into a single flake of hay. Green chopping of alfalfa in a single maneuver similarly results in trapped beetles, although they are less likely to be as concentrated than in baled forage for unavoidable consumption by livestock.

The blister beetle is the only known organism that produces cantharidin, a vesicant found primarily in the hemolymph and gonads of male beetles. Mature males synthesize the cantharidin and pass it to the females during copulation. Quantities are incorporated into eggs to deter feeding by other insects. Males of *Epicauta funebris* can synthesize up to 17 mg of cantharidin, which represents 10% of their live weight. Blister beetle preparations (gender not identified) contain 0.89% to 5.40% cantharidin dry-weight. Ingesting 5 to 6 beetles may induce colic in a horse; a lethal dose of purified cantharidin is estimated at 0.5 mg of toxin/kg body weight. Even 4 to 6 grams of beetles may be fatal. Males contain most of the cantharidin.

More than 200 species of blister beetles exist in the

Meloidae family, which is located throughout the continental United States. Members of the *Epicauta* genus are the most common beetles found in infested hay. Other common names, some of which designate specific species, are margined, black, striped, or spotted blister beetles; potato bugs; tomato bugs; and Spanish fly beetles. They are found on numerous vegetable crops, corn, oats, barley, alfalfa, sweet clover, peanuts, cotton, and soybeans and also infest weeds such as pigweed, goldenrod, goat-head, climbing milkweed, and puncturevine. The toxicity of beetle-infested hay does not always correlate with the number of beetles because cantharidin content varies in individual beetles and especially between male and female beetles; males have the highest concentration.

Blister beetles tend to aggregate in rural areas, where the swarms can range from a few hundred to thousands. The presence of large swarms of cantharidin-carrying beetles during hay harvest poses a serious problem for livestock in many agricultural areas.

The beetles are most commonly incorporated in bales of alfalfa hay or haylage. Differences in eating habits and conditions may influence the likelihood of consumption of beetles and contaminated hay. Horses are more likely to be fed in bunks or containers where they will be more likely to consume the dead beetles, whereas cattle are often fed on the ground where they have the opportunity to shake the hay, thereby avoiding consumption of dead beetles that fall to the ground. In addition, higher-quality second and third cuttings of alfalfa are most likely to be fed to horses, whereas cattle receive lower-quality first cutting of alfalfa that is unlikely to contain adult beetles,

(coyotillo, buckthorn), *Vicia villosa* (hairy vetch), *Cestrum diurnum* (day-blooming jessamine), or several others may cause significant local problems. Local extension agents, herbaria, and recent texts in the supplemental reading section are an invaluable aid to identify these plants, understand their toxicity, and prevent poisoning.

Supplemental Readings

Baker DC, Keeler RF: *Thermopsis montana*-induced myopathy in calves. J Am Vet Med Assoc 1989; 194:1269-1272.
Burrows GE, Tyrl RJ: Toxic Plants of North America, Ames, Iowa, Iowa State University Press, 2001.

Galey FD, Holstege DM, Plumlee KH et al: Diagnosis of oleander poisoning in livestock. J Vet Diagn Invest 1996; 8:358-364.
Irigoyen LF, Graca DL, Barros CSL: Experimental poisoning by *Cassia occidentalis* in horses. Pesquisa Veterinaria Brasileira (Braz J Vet Res) 1991; 11:35-44.
Kingsbury JM: Poisonous Plants of the United States and Canada, Englewood Cliffs, NY, Prentice-Hall, 1964.
Knight AP, Walter RG: A Guide to Plant Poisoning of Animals in North America, Jackson, Wyo, Teton Newmedia, 2001.
Martin BW, Terry MK, Bridges CH et al: Toxicity of *Cassia occidentalis* in the horse. Vet Hum Toxicol 1998; 23:416-417.
Spoerke DG, Murphy MM, Wruk KM et al: Five cases of *Thermopsis* poisoning. J Toxicol Clin Toxicol 1988; 26:397-406.
Thompson LJ: Depression and choke in a horse: probable white snakeroot toxicosis. Vet Hum Toxicol 1989; 31:321-322.

CHAPTER 15.4

Blister Beetle Toxicosis

STAN W. CASTEEL
TIM J. EVANS
Columbia, Missouri

Blister beetle poisoning is a cantharidin intoxication of livestock such as horses, cattle, goats, and sheep. Primarily a problem in horses, it induces severe and often fatal colic. Ruminants are less commonly affected, although they are similarly sensitive. Cantharidin poisoning also has been reported in chickens, emus, and humans. Technologic change in the way forage is harvested occurred in the 1960s and resulted in the emergence of blister beetle poisoning in livestock. The cutting and crimping of forage by a single harvesting implement (i.e., a windrower) kills and traps the beetles in hay for baling. Because these beetles swarm for mating purposes, dozens may be incorporated into a single flake of hay. Green chopping of alfalfa in a single maneuver similarly results in trapped beetles, although they are less likely to be as concentrated than in baled forage for unavoidable consumption by livestock.

The blister beetle is the only known organism that produces cantharidin, a vesicant found primarily in the hemolymph and gonads of male beetles. Mature males synthesize the cantharidin and pass it to the females during copulation. Quantities are incorporated into eggs to deter feeding by other insects. Males of *Epicauta funebris* can synthesize up to 17 mg of cantharidin, which represents 10% of their live weight. Blister beetle preparations (gender not identified) contain 0.89% to 5.40% cantharidin dry-weight. Ingesting 5 to 6 beetles may induce colic in a horse; a lethal dose of purified cantharidin is estimated at 0.5 mg of toxin/kg body weight. Even 4 to 6 grams of beetles may be fatal. Males contain most of the cantharidin.

More than 200 species of blister beetles exist in the

Meloidae family, which is located throughout the continental United States. Members of the *Epicauta* genus are the most common beetles found in infested hay. Other common names, some of which designate specific species, are margined, black, striped, or spotted blister beetles; potato bugs; tomato bugs; and Spanish fly beetles. They are found on numerous vegetable crops, corn, oats, barley, alfalfa, sweet clover, peanuts, cotton, and soybeans and also infest weeds such as pigweed, goldenrod, goat-head, climbing milkweed, and puncturevine. The toxicity of beetle-infested hay does not always correlate with the number of beetles because cantharidin content varies in individual beetles and especially between male and female beetles; males have the highest concentration.

Blister beetles tend to aggregate in rural areas, where the swarms can range from a few hundred to thousands. The presence of large swarms of cantharidin-carrying beetles during hay harvest poses a serious problem for livestock in many agricultural areas.

The beetles are most commonly incorporated in bales of alfalfa hay or haylage. Differences in eating habits and conditions may influence the likelihood of consumption of beetles and contaminated hay. Horses are more likely to be fed in bunks or containers where they will be more likely to consume the dead beetles, whereas cattle are often fed on the ground where they have the opportunity to shake the hay, thereby avoiding consumption of dead beetles that fall to the ground. In addition, higher-quality second and third cuttings of alfalfa are most likely to be fed to horses, whereas cattle receive lower-quality first cutting of alfalfa that is unlikely to contain adult beetles,

which emerge later in the growing season. Beetles also have been found in Bermuda-grass hay in Oklahoma, and cantharidin has been found in alfalfa pellets.

MECHANISMS OF ACTION OF CANTHARIDIN

First isolated in 1810, cantharidin ($C_{10}H_{12}O_4$) is a very stable substance that is soluble in oil but not water. Cantharidin is rapidly absorbed and excreted in the urine. It has an indirect action on membranes by interfering with oxidative enzymes bound to mitochondrial membranes. When these enzyme systems fail, the transport across the plasma membrane ceases with the death of the cell because of marked permeability changes in the cell membrane. Disruption of cell membranes results in acantholysis and vesicle formation. Studies of cantharidin in rodent models have resulted in the isolation and characterization of a cantharidin-binding protein from mouse liver cytosol. Inhibition of a protein phosphatase activity may partially account for the toxicity of cantharidin. At the macroscopic level, changes in the gastrointestinal tract mucosa disrupt the transfer of fluids, nutrients, and electrolytes across the mucosal barrier.

CANTHARIDIN TOXICOSIS

Once it is ingested via blister beetle-infested hay, cantharidin produces inflammation, necrosis, and ulceration of the mucosa of those portions of the gastrointestinal tract that come in direct contact with the toxin, thus potentially affecting areas from mouth to large bowel. Cantharidin causes blistering, ulcerations, and erosions of mucosal surfaces equal to a second-degree burn. It is also a powerful irritant of the urinary tract. Additional effects of the toxin are nausea, kidney dysfunction, liver degeneration, myocardial damage, hypersalivation, rapid respiration and heart rate, difficulty in swallowing, convulsions, delirium, shock, and death.

Clinical Presentation

The most obvious clinical signs of blister beetle poisoning are associated with the abrupt onset of colic: restlessness, sweating, pawing, grunting, trembling, irritable—sometimes aggressive—behavior, and an increased heart and respiratory rate. The victim is often depressed, with fever, hypersalivation and frequent urination or straining to urinate small volumes. The urine may be blood red and may even contain blood clots. Sometimes central nervous system dysfunction occurs along with signs such as head-pressing, disorientation, and apathy. Affected horses occasionally display a stiff, short-strided gait that may resemble signs of acute myositis. Evaluation of 70 cases of blister beetle poisoning in equids revealed the following: mortality was 50%; onset of signs was rapid; most had signs of gastrointestinal distress; less than 10% had neurologic signs; all that died were in terminal shock; and duration of clinical signs ranged from 3 to 18 hours. Synchronous diaphragmatic flutter in association with the hypocalcemia was reported in two of the cases. Six of the horses that died had no gross lesions, whereas only 14 had

moderate erythema of the gastrointestinal tract. Only two horses had lesions in the urinary tract.

Case Examples

Cantharidin intoxication was suspected in a 2-year-old Quarter Horse mare whose stablemate was found dead. She presented with polyuria, stranguria, fever, increased heart and respiratory rates, cyanotic mucus membranes, and decreased gastrointestinal sounds. The mare urinated small amounts of bloody, dilute urine every 5 minutes. Her serum calcium was 4.79 mg/dl. Urine cantharidin level was 280 ppb. Blister beetles, *Epicauta atrivittata*, were found in the hay. Treatment began with mineral oil, fluids, and flunixin meglumine. By the second day, she was depressed and had brick red mucus membranes, oral irritation, and laminitis with pain and sweating. Her serum calcium dropped to 3.91 mg/dl. Phenylbutazone was administered, and the mare went down in 30 minutes; calcium gluconate given orally had her up in minutes. Therapy continued for a week; she survived.

In all, 6 of 25 horses in a barn developed anorexia, fever, and colic; immersed their muzzles in water containers; frequently urinated; and had oral ulcers. Three of the six horses had mild azotemia; two had proteinuria and hematuria; and one was hypocalcemic. Cantharidin was detected in the urine. One horse died despite therapy. Blister beetle contamination ranged from zero in several alfalfa hay flakes to 15 beetles in one flake.

Diagnostic Testing

Evidence in support of a diagnosis includes a history of alfalfa consumption, signs and lesions consistent with severe gastrointestinal and urinary tract irritation, depressed serum calcium and magnesium, and chemical detection of cantharidin in gastrointestinal contents, urine or serum. Identification of cantharidin in biologic samples is the most important piece of evidence required for definitive diagnosis of cantharidin toxicosis in horses with colic. A marked and sustained reduction in serum calcium and magnesium lasting over 48 hours helps to differentiate cantharidin toxicosis from other colic-like conditions. Cantharidin concentrations in urine range from 5 to 1800 parts per billion (ppb); in gut contents, concentrations range from 21 to 4800 ppb. Clinical pathology findings may include sustained hypocalcemia (serum calcium concentration 6-8 mg/dl; normal is 10.4-13.4 mg/dl) and hypomagnesemia (serum magnesium concentration is 0.75-1.6 mg/dl; normal is 1.8-2.7 mg/dl). Hemoconcentration and azotemia with increased BUN and creatinine levels suggest cantharidin-induced renal damage.

Necropsy reveals minimal lesions in most cases, but gastrointestinal irritation is most often present. In horses, esophagitis, gastroenteritis, and erosions of the mucosa occur. In some cases, urinary tract irritation is manifested as hyperemia and hemorrhage in the renal pelvis, ureters, and bladder.

Therapy

The immediate treatment for blister beetle poisoning is administration of mineral oil and activated charcoal to min-

imize absorption of the toxin and hasten elimination; no specific antidote exists. Analgesics such as flunixin meglumine (500 mg IV) can be given for pain. Electrolyte and acid-base imbalance should be corrected with up to 30 to 40 liters of fluids that contain HCO_3 and calcium borogluconate. Systemically administered glucocorticoids may help protect against the onset of shock and relieve the irritation. Treatment may require several days. In a retrospective study of 70 cases of blister beetle poisoning in equids, 51% survived with aggressive therapy for 5 to 14 days.

Prognosis

The prognosis for recovery is directly related to the dose of cantharidin ingested. If a high dose is consumed, any delay in the treatment regimen is likely to result in mortality. However, many horses survive with the aid of early, aggressive therapy. A lethal intoxication brings about death within 24 hours, usually in 3 to 18 hours. Horses that survive for three days usually recover.

If cantharidin toxicosis is suspected, the contaminated hay should be discarded. It is a common misconception that ruminants can tolerate cantharidin; feeding contaminated forage to them will not obviate the loss.

Prevention and Control

Preventing blister beetle poisoning requires careful management of the hay supply and control of the infesting insects. Clients should learn to identify blister beetles and should know that adults emerge and congregate for mating purposes in June and July. Hay must be thoroughly inspected before it is fed to horses; beetles may be concentrated in only part of the bale. Removal of the beetle bodies does not render the surrounding hay safe; when the beetles are crushed, cantharidin may contaminate the hay.

Blister beetles tend to congregate in late summer for mating (June in the southern United States); thus early hay cuttings pose less risk. The beetles are attracted to flowers, but they also eat leaves. Therefore alfalfa should be cut before it reaches full bloom stage, and the number of flowering weeds in the hay field should be reduced. Hay

fields, especially the field margins, should be inspected for the presence of beetles. If beetles are identified in an area, harvesting there should be avoided. Modern harvesting methods of cutting and crimping lead to beetle intoxications. Crimping traps the beetles in the hay, whereas mowing without crimping allows them to escape before baling. To prevent tractor tires crushing escaping blister beetles, a harvester with wide-set wheels that windrows the hay as it is cut should be used. The live beetles then scatter before the hay baler can capture them.

Organophosphate and carbamate insecticides can be used to control blister beetles. Because the larvae of poisonous species of *Epicauta* feed on grasshopper and cricket eggs, grasshopper populations should be controlled. Following insecticide applications, forage harvesting must be delayed according to label instructions. Clients who do not raise their own hay must know and trust their hay dealers and should become familiar with dealers' hay management practices.

Supplemental Readings

- Butler L, Kitchen D: A case of blister beetle poisoning in a horse. *Southwestern Vet* 1987; 38:13-15.
- Helman RG, Edwards WC: Clinical features of blister beetle poisoning in equids: 70 cases (1983-1996). *J Am Vet Med Assoc* 1997; 211:1018-1021.
- Li YM, Casida JE: Cantharidin-binding protein: identification as protein phosphatase 2A. *Proceedings of the National Academy of Science*, vol 89, pp 11869-11870, 1992.
- Ray AC, Kyle AL, Murphy MJ et al: Etiologic agents, incidence, and improved diagnostic methods of cantharidin toxicosis in horses. *Am J Vet Res* 1989; 50:187-191.
- Ray AC, Tamulinas SH, Reagor JC: High-pressure liquid chromatographic determination of cantharidin, using a derivatization method in specimens from animals acutely poisoned by ingestion of blister beetles, *Epicauta lemniscata*. *Am J Vet Res* 1979; 40:498-504.
- Rollins JB: Blister beetle poisoning in horses. *Equine Pract* 1985; 7:6-8.
- Schmitz DG: Cantharidin toxicosis in horses. *J Vet Intern Med* 1989; 3:208-215.
- Shawley RV, Rolf LL Jr: Experimental cantharidiasis in the horse. *Am J Vet Res* 1984; 45:2261-2266.

CHAPTER 15.5

Berteroa incana Toxicosis

WILSON K. RUMBEIHA

East Lansing, Michigan

Berteroa incana is the most common cause of toxin-induced laminitis in Michigan horses. This weed is native to Europe, Asia, and is now well established in North America. It is commonly found in the Northeast and Upper Midwestern states and parts of Canada. Although it was first recognized as a cause of equine laminitis 10 years ago, the toxicity of this plant is still widely unknown among veterinarians and animal owners. *B. incana* is known commonly as *hoary alyssum* or *hoary false alyssum*. An annual or biannual plant, *B. incana* grows to a height of 4 to 30 in. The plant is commonly found in disturbed and waste lands, roadsides or railroads, and in overgrazed hay fields, and may predominate in hay fields during drought seasons as the result of its drought resistance. This weed may also outgrow other plant species after herbicide applications. *B. incana* is not highly palatable and is therefore avoided by most livestock; thus it is more likely to cause problems when it is abundant in pasture. The toxicity of this weed has been demonstrated to last as long as 9 months in hay, but no specific studies exist that have examined the safety of contaminated hay after this period. Therefore hay with more than 15% *B. incana* should be avoided.

Most of the cases of *B. incana* poisoning in Michigan are seen from May to September following ingestion of the fresh plants on pasture. Almost all cases in Michigan are reported in the lower third of the Lower Michigan Peninsula. A few cases have been associated with ingestion of contaminated hay ingested between October and December. *B. incana* toxicosis has been reported in other states including Minnesota and Florida. In the Florida case, it is speculated that contaminated hay was purchased from another state. For this reason, veterinarians in states where this weed does not naturally grow should be aware that hay purchased from other states may contain the plant. Horses are the only livestock currently known to be affected by this weed.

CLINICAL SIGNS

The most dramatic clinical sign of *B. incana* toxicity is "stocking up." This is pitting edema and laminitis of one or more limbs. This condition develops within 12 to 24 hours after horses have had access to a pasture or hay contaminated by at least 10% to 15% of this weed. Affected horses will stand in a laminitic stance with forelimbs extended, and they will be reluctant to walk, especially on hard surfaces. The limbs feel warm and have strong and fast digital pulses. Horses will have increased sensitivity to the hoof tester. The majority of the affected horses have

low to midgrade fever. Some horses may have diarrhea and dehydration.

There appears to be a dose-response relationship to *B. incana* with horses that ingest hay containing more than 60% of this weed showing some of the most severe signs. These severe signs include foundering, bloody diarrhea, and passing brown-colored urine. Male horses may develop scrotal edema.

Pregnant horses appear to be the most sensitive to *B. incana* toxicity. This may be due to altered physiological status or altered toxicokinetics of the toxin. Broodmare horses intoxicated by this weed have had premature deliveries (300-321 days of gestation) without prior signs of impending delivery or late-term (9-10 month) abortions. Other signs noted in a group of broodmare horses which ingested contaminated hay containing 10% to 40% *B. incana* included fever, colic, dehydration, tachycardia, tachypnea, and moderate to profuse bloody diarrhea.

For all clinical signs, the morbidity rate is approximately 50% for animals ingesting hay that contains 30% to 70% *B. incana*. Complications of *B. incana* poisoning include rotation of the third phalanx—a condition that usually occurs if the affected animal is not rested and continues to ingest contaminated hay or pasture. Other clinical signs observed include hematuria and renal failure. Death has been reported in horses that ingest hay that contains this weed.

MECHANISM OF ACTION

The toxic chemical in *B. incana* has not yet been identified; therefore the mechanism of action is not known. Perivascular edema has been reported histologically and suggests increased vascular permeability as a possible mechanism of action. In cases of premature delivery, the placenta has been found intact. Therefore the placenta appears not to be the target organ of *B. incana* toxin, so the cause of these reproductive problems remains unexplained.

DIAGNOSIS

The diagnosis of *B. incana* poisoning in horses is currently based on the clinician's observation of clinical signs and location of the offending weed. No chemical analytical methods exist to support a diagnosis of exposure to *B. incana* because the chemical toxin is not known. Also no hematology or chemistry profile exists that is diagnostic of *B. incana* toxicosis. Gross pathologic findings associated with *B. incana* poisoning include edema of the subcutaneous tissues, lungs, and kidneys, and in some cases

perirenal edema and hemorrhage are evident. Hemothorax and ecchymotic hemorrhages have also been reported. The mucosa of the small intestines may be inflamed and hemorrhagic in the most severely affected animals. Black walnut poisoning is the major differential for *B. incana* toxicosis.

TREATMENT

The disease is usually not life-threatening. The offending hay should be removed immediately. If the horse is on pasture it should be immediately moved to a better pasture. Treatment of *B. incana* toxicosis is supportive and primarily directed towards pain relief, and treatment of edema and inflammation. Edema is treated with diuretics, and inflammation is treated with phenylbutazone and flunixin meglumine. Cool water hydrotherapy of the affected limbs is also recommended. Sucralfate or other gastrointestinal protectants should be given as needed. These treatment modalities should be given in conjunction with complete rest. Horses that are mildly to moderately affected usually recover 2 to 4 days after this therapy is initiated.

CONTROL OF *BERTEROA INCANA*

This weed grows in disturbed or overgrazed pastures; therefore, control should involve proper pasture management including controlled grazing. Although herbicides like 2,4-D or hexazinone have been shown to suppress this weed in grass pastures, consultation with local pesticide applicators should indicate the product and application rates allowable in a particular case.

Supplemental Readings

- Becker RL, Martin NP, Murphy MJ: Hoary alyssum: toxicity to horses, forage quality, and control [fact sheet], St Paul, Minn, University of Minnesota Extension Service, 1991.
- Burrows GE, Tyrl RJ: Brassicaceae burnett. In Burrows GE, Tyrl RJ (eds): Toxic Plants of North America, pp 282-308, Ames, Iowa, Iowa State University Press, 2001.
- Ellison SP: Possible toxicity caused by hoary alyssum (*Berteroa incana*). Vet Med 1992; 87:472-475.
- Geor RJ, Becker RL, Kanara EW et al.: Toxicosis in horses after ingesting hoary alyssum. J Am Vet Med Assoc 1992; 201:63-67.
- Hovda LR, Rose ML: Hoary alyssum (*Bertorea incana*) toxicity in a herd of broodmare horses. Vet Hum Toxicol 1993; 35:39-40.

CHAPTER 15.6

Pyrrolizidine Alkaloid Poisoning

PATRICIA TALCOTT
Moscow, Idaho

Pyrrolizidine alkaloids (PAs) are a group of structurally similar compounds found in more than 6000 species of plants worldwide. Many of these alkaloids have been well described and tested for their toxicity; some are hepatotoxic and others are not. Within the United States six primary genera of plants contain hepatotoxic PAs—*Senecio*, *Amsinckia*, *Cynoglossum*, *Crotalaria*, *Heliotropium*, and *Echium*. Poisonings in horses after consumption of PA plants do not occur as often now as it did 20 years ago. This decrease in frequency is most likely the result of widespread recognition of the problem and use of effective livestock management practices by producers. In addition, certain biologic control measures have been used fairly effectively to control the spread of dense populations of some of these toxic plant species.

TOXIC DOSE

No sex or breed predilection in horses for the development of this disease has been identified. It has been suggested that younger animals might be more susceptible because this poisoning was reported in a 2-month-old foal whose mother grazed on *Senecio* spp. plants during preg-

nancy. Because most parts of the plants are poisonous and are toxic either fresh or dried, poisonings in horses from pasture grazing or ingestion of contaminated hay or grain can be seen at any time of the year. Acute poisonings with these plants is extremely rare because of the tremendous amount of plant material a horse would have to ingest within a relatively short period of time. The large majority of poisonings documented in horses occur after chronic exposures, with exposure times of from 2 weeks to several months. Factors that affect exposure times include specific plant ingested, part(s) of the plant ingested, stage of maturity of the plant, total dose, and environmental factors that affect plant growth and production of the PAs. Management practices may also affect the incidence and severity of disease, because most PA-containing plants are not considered to be palatable to livestock.

Approximately 25 species of *Senecio* plants exist in the United States that have been identified as being potentially hepatotoxic. These plants can inhabit quite diverse environmental habitats and can be annuals, biennials, or perennials. Because poisonings are a result of excessive intake during a period of from weeks to months, those plants that present the greatest health risk to horses are

perirenal edema and hemorrhage are evident. Hemothorax and ecchymotic hemorrhages have also been reported. The mucosa of the small intestines may be inflamed and hemorrhagic in the most severely affected animals. Black walnut poisoning is the major differential for *B. incana* toxicosis.

TREATMENT

The disease is usually not life-threatening. The offending hay should be removed immediately. If the horse is on pasture it should be immediately moved to a better pasture. Treatment of *B. incana* toxicosis is supportive and primarily directed towards pain relief, and treatment of edema and inflammation. Edema is treated with diuretics, and inflammation is treated with phenylbutazone and flunixin meglumine. Cool water hydrotherapy of the affected limbs is also recommended. Sucralfate or other gastrointestinal protectants should be given as needed. These treatment modalities should be given in conjunction with complete rest. Horses that are mildly to moderately affected usually recover 2 to 4 days after this therapy is initiated.

CONTROL OF *BERTEROA INCANA*

This weed grows in disturbed or overgrazed pastures; therefore, control should involve proper pasture management including controlled grazing. Although herbicides like 2,4-D or hexazinone have been shown to suppress this weed in grass pastures, consultation with local pesticide applicators should indicate the product and application rates allowable in a particular case.

Supplemental Readings

- Becker RL, Martin NP, Murphy MJ: Hoary alyssum: toxicity to horses, forage quality, and control [fact sheet], St Paul, Minn, University of Minnesota Extension Service, 1991.
- Burrows GE, Tyrl RJ: Brassicaceae burnett. In Burrows GE, Tyrl RJ (eds): Toxic Plants of North America, pp 282-308, Ames, Iowa, Iowa State University Press, 2001.
- Ellison SP: Possible toxicity caused by hoary alyssum (*Berteroa incana*). Vet Med 1992; 87:472-475.
- Geor RJ, Becker RL, Kanara EW et al.: Toxicosis in horses after ingesting hoary alyssum. J Am Vet Med Assoc 1992; 201:63-67.
- Hovda LR, Rose ML: Hoary alyssum (*Bertorea incana*) toxicity in a herd of broodmare horses. Vet Hum Toxicol 1993; 35:39-40.

CHAPTER 15.6

Pyrrolizidine Alkaloid Poisoning

PATRICIA TALCOTT
Moscow, Idaho

Pyrrolizidine alkaloids (PAs) are a group of structurally similar compounds found in more than 6000 species of plants worldwide. Many of these alkaloids have been well described and tested for their toxicity; some are hepatotoxic and others are not. Within the United States six primary genera of plants contain hepatotoxic PAs—*Senecio*, *Amsinckia*, *Cynoglossum*, *Crotalaria*, *Heliotropium*, and *Echium*. Poisonings in horses after consumption of PA plants do not occur as often now as it did 20 years ago. This decrease in frequency is most likely the result of widespread recognition of the problem and use of effective livestock management practices by producers. In addition, certain biologic control measures have been used fairly effectively to control the spread of dense populations of some of these toxic plant species.

TOXIC DOSE

No sex or breed predilection in horses for the development of this disease has been identified. It has been suggested that younger animals might be more susceptible because this poisoning was reported in a 2-month-old foal whose mother grazed on *Senecio* spp. plants during preg-

nancy. Because most parts of the plants are poisonous and are toxic either fresh or dried, poisonings in horses from pasture grazing or ingestion of contaminated hay or grain can be seen at any time of the year. Acute poisonings with these plants is extremely rare because of the tremendous amount of plant material a horse would have to ingest within a relatively short period of time. The large majority of poisonings documented in horses occur after chronic exposures, with exposure times of from 2 weeks to several months. Factors that affect exposure times include specific plant ingested, part(s) of the plant ingested, stage of maturity of the plant, total dose, and environmental factors that affect plant growth and production of the PAs. Management practices may also affect the incidence and severity of disease, because most PA-containing plants are not considered to be palatable to livestock.

Approximately 25 species of *Senecio* plants exist in the United States that have been identified as being potentially hepatotoxic. These plants can inhabit quite diverse environmental habitats and can be annuals, biennials, or perennials. Because poisonings are a result of excessive intake during a period of from weeks to months, those plants that present the greatest health risk to horses are

those that grow in dense stands and perhaps have long growing seasons. *Senecio vulgaris* (common groundsel), *Senecio jacobaea* (tansy ragwort), *Senecio flaccidus* (thread-leaf groundsel), and *Senecio riddellii* (Riddell's groundsel) are the four plants that have presented the greatest toxic threat to livestock. Ingestion of plant material at a level of 1% to 5% body weight daily will potentially cause hepatic disease after weeks of exposure. Sometimes as much as 50% body weight is required before clinical signs develop. Some literature has suggested that a chronic lethal dose of tansy ragwort for horses is 0.05 to 0.20 kg plant material/kg body weight daily. In this author's experience, common groundsel has been responsible for most of the poisonings in horses in the Pacific Northwest.

Of the several *Cynoglossum* species present in the United States, only *Cynoglossum officinale* (hound's-tongue) has been specifically implicated as causing hepatic disease. Hound's-tongue can form very dense stands in a wide range of habitats, and has spread throughout most of the United States and Canada. Ingestion of 1 dried hound's-tongue plant per day for 2 weeks can cause clinical disease in a 500-kg horse.

Poisonings with *Amsinckia* spp., *Crotalaria* spp., *Heliotropium* spp., and *Echium* spp. occur rarely in horses in the United States, most likely as the result of a combination of reasons including lack of palatability and relatively discrete small populations of plant material localized in any one location.

MECHANISM OF ACTION

In most plants, the highest concentrations of PAs are present in the seeds, inflorescences, and young, new growth. After rapid absorption from the gastrointestinal tract, the liver converts these alkaloids to highly reactive alkylating pyrroles that bind to deoxyribonucleic acid, ribonucleic acid, and other cellular proteins. The major target organ is the liver, with the lung and kidney less commonly affected. Clinical signs of disease are primarily associated with the hepatic changes characterized by hepatocellular necrosis, biliary hyperplasia, fibrosis, and hepatocytomegaly and karyomegaly. Neurologic signs are attributed to hepatoencephalopathy. Terminally, one may also see a hemolytic event sometimes associated with end-stage liver disease in horses.

Some of the PAs have been shown to cross the placenta as well as into the milk, thus posing a risk (albeit negligible) to the developing fetus or newborn.

CLINICAL SIGNS

The majority of affected horses suffer from subtle, chronic weight loss and general debilitation associated with hepatic insufficiency. Other reported signs may include weakness, depression, ataxia, icterus, and secondary photosensitivity. In the "chronic-delayed form" of the disease, clinical signs can appear quite suddenly even though the exposure and liver lesions have been chronic and progressive. Food intake and nutritional status can also modify the effects of PAs; high-protein diets have been shown to be somewhat protective in preventing this disease. Most affected patients, particularly those suffering from the

chronic-delayed form, exhibit neurologic signs attributed to a hepatoencephalopathy that include mania, derangement, yawning, aimless walking, head-pressing, drowsiness, blindness, and ataxia. Signs can occur abruptly after a stressful event such as transport or parturition. Edema, gastric impaction, inspiratory dyspnea, laryngeal and pharyngeal paralysis, and diarrhea with tenesmus, have also been reported less commonly in afflicted horses.

DIAGNOSIS

The diagnosis of PA poisoning is based on compatible clinical signs, clinical pathologic abnormalities, histologic lesions, and evidence of ingestion of pyrrolizidine-containing plants at some point in the recent past. Common blood changes include significant elevations in γ -glutamyl transferase, alkaline phosphatase, aspartate aminotransferase, and bile acids, hyperbilirubinemia, hypoproteinemias (hypoalbuminemia), hyperammonemia, and an inflammatory leukogram. Liver function tests are generally markedly prolonged.

The liver examined through either ultrasound or necropsy tends to be small, pale, and firm, with a mottled, cut surface. Common histologic features (extent and severity of the lesions can vary) include megalocytosis with mild necrosis, centrilobular and periportal fibrosis, and biliary hyperplasia. Other less recognized lesions include myocardial necrosis, cecal and colonic edema and hemorrhage, adrenal cortical hypertrophy, interstitial pneumonia, and brain status spongiosus.

PA plants can be difficult to identify in gastrointestinal contents, but can be more readily identified through examination of the total diet. This includes examination of the grain, hay, silage, haylage, and pasture. Pyrrole analysis of blood and liver tissue is only offered by a few laboratories, and is not commonly done on suspect cases.

TREATMENT

No specific treatments exist for this disease. Many treatments for horses with hepatic disease have been tried with limited success. The primary goal in treatment is to provide maintenance therapy and general nursing care until enough liver tissue can regenerate and function adequately to support that individual patient's lifestyle. Most PA poisoned patients respond poorly to treatment because by the time the disease is diagnosed, adequate regeneration of the liver is not possible. Plenty of rest with reduction of stress is important. The following is a synopsis of treatment options that have been described elsewhere.

Administration of IV fluids to correct dehydration is often necessary. Glucose may be added to provide adequate energy needs. Photodermatitis can be successfully treated with basic topical wound therapy management protocols and use of broad-spectrum antibiotics (e.g., cephalosporins) and avoidance of direct sunlight.

Diets should be high calorie, highly digestible, and low in protein. One suggested diet includes 1 to 2 parts beet pulp and up to 1 part cracked corn mixed with molasses and fed at a rate of 2.5 kg/100 lb body weight daily. Sorghum or milo can be substituted for the beet pulp. Oat or grass hay is a good source of roughage. Oral pastes and

IV preparations with high concentrations of branched-chain amino acids and antioxidants have been used with questionable success. Weekly vitamin B₁, folic acid, and vitamin K₁ supplementation should be considered.

Horses that display neurologic signs may require diazepam (foals, 0.05-0.4 mg/kg IV; adults, 25-50 mg IV; may be necessary to repeat) or xylazine (1.1 mg/kg IV or 2.2 mg/kg intramuscular). Oral neomycin (50-100 mg/kg q6h for 1 day), lactulose (0.3 ml/kg q6h), or mineral oil have been used in an attempt to decrease blood ammonia concentrations with varying results. Diarrhea is a common sequelae after either neomycin or lactulose therapy. Neomycin administration can also predispose the patient to salmonellosis. The clinician should take care when determining dosages for any medication that undergoes extensive hepatic metabolism, either for activation or detoxification.

Pneumonia and chronic wasting are the most commonly described long-term sequelae associated with this poisoning. The prognoses for most patients are poor, and many are euthanized because of severe debilitation or nonresponsive neurologic signs. A few animals do recover after several months of care but are not usually able to regain their former fitness or activity level.

Supplemental Readings

- Barton MH, Morris DD: Diseases of the liver. In Reed SM, Bayly WM (eds): *Equine Internal Medicine*, Philadelphia, WB Saunders Company, 1998.
- Burrows GE, Tyrl RJ: *Senecio* L. In Burrows GE, Tyrl RJ (eds): *Toxic Plants of North America*, p 193, Ames, Iowa, Iowa State University Press, 2001.
- Craig AM, Pearson EG, Meyer C et al: Clinicopathologic studies of tansy ragwort toxicosis in ponies: sequential serum and histopathological changes. *Equine Vet Sci* 1991; 11(5):26.
- Craig MA, Pearson EG, Meyer C et al: Serum liver enzyme and histopathologic changes in calves with chronic and chronic-delayed *Senecio jacobae* toxicosis. *Am J Vet Res* 1991; 52:1969-1978.
- Divers TJ: Therapy of liver failure. In Smith BP (ed): *Large Animal Internal Medicine*, St Louis, Mosby, 1990.
- Mendel VE, Witt MR, Gitchell BS et al: Pyrrolizidine alkaloid-induced liver disease in horses: an early diagnosis. *Am J Vet Res* 1998; 49:572.
- Small AC, Kelly WR, Seawright AA et al: Pyrrolizidine alkaloidosis in a two-month-old foal. *Zentralbl Veterinarmed A* 1993; 40:213-218.
- Stegelmeier BL, Gardner DR, James LF et al: Pyrrole detection and the pathologic progression of *Cynoglossum officinale* (hound's-tongue) poisoning in horses. *J Vet Diagn Invest* 1996; 8:81-90.

CHAPTER 15.7

Alsike Clover (*Trifolium hybridum*) and Red Clover (*Trifolium pratense*) Poisoning

PATRICIA TALCOTT

Moscow, Idaho

Poisoning with alsike clover (*Trifolium hybridum*) and red clover (*Trifolium pratense*) in horses has historically been referred to as *big liver disease*, *dew poisoning*, or *trifoliosis*. In the Northwest, ingestion of both these plants in horses has been associated with acute or chronic hepatic dysfunction, along with secondary photosensitivity. Both alsike and red clover are in the Fabaceae family. They are both very hardy and palatable plants and have been quite popular additions to equine pasture seed mixes. They thrive in many soil types, particularly in more cool and moderate climates.

Alsike clover typically has erect stems that grow as high as 3 feet. The plant has a trifoliate leaf pattern, with each individual oval leaflet as long as 1 inch with serrations along the margins. The single flowers are pink/white globose heads that grow as long as 1 inch.

Red clover also has erect stems 1 to 3 feet tall with a tri-

foliate leaf pattern. The leaflets are typically oval, hairy, 1 to 2.5 inches long, and often have a "water mark" (inverted V) on the upper surface. Red clover has large, broad stipules and the flowers are rose/purple/red globose heads that grow as long as 1 inch.

TOXIC DOSE

The hepatotoxin responsible for this disease in horses is unknown. A hepatotoxic mycotoxin is an attractive hypothetical causative agent because the mold *Cymodothea trifolii* has been identified on these clovers in outbreaks of clinical disease. Other evidence that supports a mycotoxin as the culprit is that the incidence of disease in horses is quite variable from year to year, with most cases in the Northwest occurring in horses between April and November when the spring has been long and wet. Poisonings,

IV preparations with high concentrations of branched-chain amino acids and antioxidants have been used with questionable success. Weekly vitamin B₁, folic acid, and vitamin K₁ supplementation should be considered.

Horses that display neurologic signs may require diazepam (foals, 0.05-0.4 mg/kg IV; adults, 25-50 mg IV; may be necessary to repeat) or xylazine (1.1 mg/kg IV or 2.2 mg/kg intramuscular). Oral neomycin (50-100 mg/kg q6h for 1 day), lactulose (0.3 ml/kg q6h), or mineral oil have been used in an attempt to decrease blood ammonia concentrations with varying results. Diarrhea is a common sequelae after either neomycin or lactulose therapy. Neomycin administration can also predispose the patient to salmonellosis. The clinician should take care when determining dosages for any medication that undergoes extensive hepatic metabolism, either for activation or detoxification.

Pneumonia and chronic wasting are the most commonly described long-term sequelae associated with this poisoning. The prognoses for most patients are poor, and many are euthanized because of severe debilitation or nonresponsive neurologic signs. A few animals do recover after several months of care but are not usually able to regain their former fitness or activity level.

Supplemental Readings

- Barton MH, Morris DD: Diseases of the liver. In Reed SM, Bayly WM (eds): *Equine Internal Medicine*, Philadelphia, WB Saunders Company, 1998.
- Burrows GE, Tyrl RJ: *Senecio* L. In Burrows GE, Tyrl RJ (eds): *Toxic Plants of North America*, p 193, Ames, Iowa, Iowa State University Press, 2001.
- Craig AM, Pearson EG, Meyer C et al: Clinicopathologic studies of tansy ragwort toxicosis in ponies: sequential serum and histopathological changes. *Equine Vet Sci* 1991; 11(5):26.
- Craig MA, Pearson EG, Meyer C et al: Serum liver enzyme and histopathologic changes in calves with chronic and chronic-delayed *Senecio jacobae* toxicosis. *Am J Vet Res* 1991; 52:1969-1978.
- Divers TJ: Therapy of liver failure. In Smith BP (ed): *Large Animal Internal Medicine*, St Louis, Mosby, 1990.
- Mendel VE, Witt MR, Gitchell BS et al: Pyrrolizidine alkaloid-induced liver disease in horses: an early diagnosis. *Am J Vet Res* 1998; 49:572.
- Small AC, Kelly WR, Seawright AA et al: Pyrrolizidine alkaloidosis in a two-month-old foal. *Zentralbl Veterinarmed A* 1993; 40:213-218.
- Stegelmeier BL, Gardner DR, James LF et al: Pyrrole detection and the pathologic progression of *Cynoglossum officinale* (hound's-tongue) poisoning in horses. *J Vet Diagn Invest* 1996; 8:81-90.

CHAPTER 15.7

Alsike Clover (*Trifolium hybridum*) and Red Clover (*Trifolium pratense*) Poisoning

PATRICIA TALCOTT

Moscow, Idaho

Poisoning with alsike clover (*Trifolium hybridum*) and red clover (*Trifolium pratense*) in horses has historically been referred to as *big liver disease*, *dew poisoning*, or *trifoliosis*. In the Northwest, ingestion of both these plants in horses has been associated with acute or chronic hepatic dysfunction, along with secondary photosensitivity. Both alsike and red clover are in the Fabaceae family. They are both very hardy and palatable plants and have been quite popular additions to equine pasture seed mixes. They thrive in many soil types, particularly in more cool and moderate climates.

Alsike clover typically has erect stems that grow as high as 3 feet. The plant has a trifoliate leaf pattern, with each individual oval leaflet as long as 1 inch with serrations along the margins. The single flowers are pink/white globose heads that grow as long as 1 inch.

Red clover also has erect stems 1 to 3 feet tall with a tri-

foliate leaf pattern. The leaflets are typically oval, hairy, 1 to 2.5 inches long, and often have a "water mark" (inverted V) on the upper surface. Red clover has large, broad stipules and the flowers are rose/purple/red globose heads that grow as long as 1 inch.

TOXIC DOSE

The hepatotoxin responsible for this disease in horses is unknown. A hepatotoxic mycotoxin is an attractive hypothetical causative agent because the mold *Cymodothea trifolii* has been identified on these clovers in outbreaks of clinical disease. Other evidence that supports a mycotoxin as the culprit is that the incidence of disease in horses is quite variable from year to year, with most cases in the Northwest occurring in horses between April and November when the spring has been long and wet. Poisonings,

however, can occur all year round because outbreaks in horses have not only been associated with pasture grazing, but also ingesting contaminated hay.

Toxicities have been reported in horses after ingestion of as little as 20% clover in their diet, especially alsike clover. In this author's experience, most cases of poisoning with red clover occur when horses ingest more than 50% of their diet as red clover. The time between ingestion and onset of clinical signs can vary from 2 to 4 weeks to several months after initial exposure before signs are observed, depending primarily on the percentage of clover in the diet.

CLINICAL SIGNS

Often the first signs of poisoning are sunburned lesions (i.e., varying degrees of erythema, edema, ulceration, necrosis, and sloughing) of the nonpigmented areas of the skin in addition to the cornea and mucous membranes. These lesions are a result of a secondary photosensitivity, and respond quite favorably to basic wound therapy, removal of the animal from direct sunlight, and eliminating the offending clover from the diet.

When these lesions are not apparent (in darkly pigmented horses) or go unrecognized, they can rapidly progress to the more common neurologic form of severe hepatic disease. Common clinical signs include yawning, ataxia, head pressing, loss of appetite, aimless wandering, incoordination, grinding of the teeth, and a rather abrupt onset of depression. Other less commonly reported signs include colic, blindness, and inability to prehend or swallow food. The disease can rapidly progress to include recumbency, seizures, and death. The chronic or cachexic form of the disease is less commonly recognized and includes a decrease in appetite, poor body condition and hair coat, and progressive wasting.

DIAGNOSIS

The diagnosis is commonly made through a combination of compatible clinical signs of photosensitivity and hepatic dysfunction, clinical pathologic abnormalities suggestive of hepatic disease, histologic lesions (antemortem biopsy or postmortem examination), and confirmation of either red clover or alsike clover in the diet.

The majority of alsike- and red clover-poisoned patients exhibit significant elevations in γ -glutamyl transferase, alkaline phosphatase, aspartate transaminase, and

total serum bilirubin. Other abnormalities less commonly reported may include elevations in serum alanine aminotransferase, sorbitol dehydrogenase, bile acids, and serum ammonia concentrations. Icterus is not consistently observed in clinically affected horses. Hemograms and urinalyses are typically unremarkable, except for a possible bilirubinuria.

No consistent and pathognomonic liver lesions exist in poisoned horses, and the extent and severity of the lesions can be quite variable. Grossly, the liver can be normal, enlarged, or shrunken in appearance. Commonly described lesions in the liver include biliary hyperplasia and perilobular, centrilobular, and/or periportal fibrosis. The inflammation and necrosis of the parenchyma may be mild to moderate, and (rarely) lipidosis and megalocytosis are described.

TREATMENT

The photosensitivity lesions respond well to basic wound therapy (e.g., cleansing, debridement, hydrotherapy, bandaging), in addition to removing the offending diet and placing the animal in a dark environment. The horse should be kept out of direct sunlight until the liver enzyme values are nearly back to normal (approximately 1-2 weeks). Animals suffering from the nervous or cachexic form of the disease do not fare as well. These horses may benefit from good supportive nursing care including intravenous fluids, multivitamins, a low-protein, high-carbohydrate diet, and branched chain amino acids. However, the short- and long-term prognoses are usually not favorable for the nervous or cachexic form of the disease.

Supplemental Readings

- Colon JL, Jackson CA, Del Piero F: Hepatic dysfunction and photodermatitis secondary to alsike clover poisoning. *Comp Cont Educ Pract Vet* 1996; 18(9):1022.
- Murphy MJ: Secondary photosensitivity in horses ingesting *Cymodothea trifolii* infested clover. Fifth International Symposium on Poisonous Plants, pp 19-45, San Angelo, Tex, 1997.
- Talcott PA: Alsike clover (*Trifolium hybridum*) and red clover (*Trifolium pratense*) poisonings in horses. Proceedings of the 18th Annual Meeting of the American College of Veterinary Internal Medicine, p 161, 2000.

CHAPTER 15.8

Molds

MIKE MURPHY

Saint Paul, Minnesota

Moldy feed is a perceived problem with many horse owners. They may believe that all airborne particulate matter that arises from their feed or hay source is mold. In many instances this airborne particulate matter is dust from dry soil, grain, plant or insect matter. This chapter focuses on those instances in which the material is in fact the vegetative or spore form of a mold or molds.

All molds do not produce mycotoxins. Horses may experience mold-associated disease in the categories of mycoses, allergies, or mycotoxicoses. This chapter focuses on mycoses and allergies. Chapters 15.9 and 15.10 and those in previous editions discuss the mycotoxicoses.

Table 15.8-1 lists molds that have been reported in different organ systems of horses, and Table 15.8-2 provides a list of molds and mycotoxins that affect horses.

MOLD-INDUCED DISEASES

A number of diseases in horses have been associated with the presence of molds. These diseases, or mycoses, involve guttural pouches, lungs, eyes, skin, the reproductive system, and the body as a whole.

Guttural Pouch Mycosis

Molds have been isolated from infected guttural pouches in horses worldwide. Erosion of the internal carotid artery, cranial nerve damage, or blindness may follow guttural pouch mycoses (see Chapter 7.7: "Guttural Pouch Disease"). The most common molds isolated from equine guttural pouches are *Aspergillus*, *Penicillium*, and *Candida*. *Aspergillus nidulans* is the *Aspergillus* species most commonly isolated from equine guttural pouches. *Aspergillus nidulans* has recently been renamed *Emericella nidulans*.

The association between *Aspergillus nidulans* and guttural pouch mycosis was first recognized in the early 1970s. Soon thereafter an association between *Aspergillus nidulans* guttural pouch mycosis and nosebleeds was made. Horses have bled to death after erosion of the carotid artery because of *Emericella nidulans* infection of the guttural pouch.

Two other species of *Aspergillus* are commonly isolated from equine guttural pouches. *Aspergillus fumigatus* from a guttural pouch infection has caused an atlantooccipital joint infection and nasal discharge. Guttural pouch mycosis has also been caused by *Aspergillus ochraceus*. A *Penicillium* sp. mold was isolated from the guttural pouch of a

horse with a fistula that developed from a guttural pouch mycosis.

Lungs

Aspergillus organisms have also been associated with lung lesions in horses. Both acute and chronic forms of the disease have been identified. An association between GI disease and pulmonary *Aspergillosis* has also been suspected. Invasive pulmonary aspergillosis has been identified in 19 horses; 16 of them also had enterocolitis. Endocarditis, apathy, fever, lacrimation and dyspnea with thrombosis, hemorrhage and tissue necrosis have been associated with *Aspergillus niger*. The sudden death of two horses was attributed to the rapid and acute development of pulmonary aspergillosis.

Eyes

A variety of molds have been isolated from the eyes of horses with keratitis. *Alternaria*, *Aspergillus*, *Actinomyces*, *Candida*, *Fusarium*, *Penicillium*, *Mucor*, *Rhizopus*, *Cephalosporium*, and *Phycomyces* organisms have all been isolated. *Aspergillus*, *Fusarium*, and *Penicillium* organisms seem to be the most prevalent. *Aspergillus flavus*, *A. fumigatus*, and *Aspergillus oryzae* are the most commonly reported *Aspergillus* species.

Reproductive System

Molds associated with abortions or with uterine or placental infections in horses include *Candida tropicalis*, *A. fumigatus*, *Candida albicans*, *Cryptococcus laurentii*, *Mucor*, *Aspergillus*, and *Microsporum*. *A. fumigatus* has been diagnosed as the cause of abortion in two Thoroughbred mares.

A. fumigatus and *Candida albicans* have been isolated from mares with uterine infections. Fungi isolated from the uteri of mares with endometritis are *Actinomyces*, *Aspergillus*, *Candida*, *Coccidioides*, *Hansenula*, *Monosporium*, *Mucor*, *Nocardia*, *Paecilomyces*, and *Trichosporon* organisms. Of 27 mares with chronic infertility problems, *Alternaria* sp., *Aspergillus flavus*, *A. fumigatus*, *A. niger*, *Mortierella wolfii*, and *Mucor* sp. were isolated from cervical, vaginal, or clitoral fossa swabs. Of 200 cases of infective placentitis, 37 were caused by *A. fumigatus* and 14 by *Absidia* sp.

Skin

Of 1090 horses examined, most had *Trichophyton equinum* skin disease, but *Aspergillus* infection was common.

Table 15.8-1
Molds that Have Been Reported in Different Organ Systems of Horses

Mold	System/Disease	Mold	System/Disease
<i>Absidia</i> organisms	Reproductive	<i>Candida albicans</i>	Reproductive
<i>Actinomyces</i> organisms	Eyes	<i>Candida tropicalis</i>	Reproductive
	Reproductive	<i>Cephalosporium</i> organisms	Eyes
<i>Alternaria</i> organisms	Eyes	<i>Cladosporium</i> organisms	Eyes
	Reproductive	<i>Coccidioides</i> organisms	Reproductive
<i>Aspergillus</i> organisms	Eyes	<i>Cryptococcus laurentii</i>	Reproductive
	Guttural pouch disease	<i>Emericella nidulans</i>	Guttural pouch disease
	Lungs	<i>Fusarium</i> organisms	Eyes
	Reproductive	<i>Hansenula</i> organisms	Reproductive
	Skin	<i>Micropolyspora faeni</i>	Heaves
<i>Aspergillus flavus</i>	Eyes	<i>Microsporum</i> organisms	Reproductive
	Reproductive	<i>Mortierella wolfii</i>	Reproductive
	Septicemia	<i>Mucor</i> organisms	Eyes
<i>Aspergillus fumigatus</i>	Heaves		Reproductive
	Eyes		Septicemia
	Guttural pouch disease	<i>Nocardia</i> organisms	Reproductive
	Reproductive	<i>Paecilomyces</i> organisms	Reproductive
<i>Aspergillus nidulans</i>	Guttural pouch disease	<i>Penicillium</i> organisms	Eyes
<i>Aspergillus niger</i>	Lungs		Guttural pouch disease
	Reproductive	<i>Phycomyces</i> organisms	Eyes
	Septicemia	<i>Rhizopus</i> organisms	Septicemia
<i>Aspergillus ochraceus</i>	Guttural pouch disease	<i>Rhizopus stonifer</i>	Eyes
<i>Aspergillus oryzae</i>	Eyes		Lungs
<i>Candida</i> organisms	Eyes	<i>Trichophyton equinum</i>	Skin
	Guttural pouch disease	<i>Trichosporon</i> organisms	Reproductive
	Reproductive		

Table 15.8-2
Molds and Mycotoxins that Affect Horses

Mold	Source	Mycotoxin
<i>Acromonium coenophialum</i>	Fescue	Ergovaline
<i>Aspergillus</i> organisms	Grain	Aflatoxin
<i>Claviceps purpurea</i>	Small grains	Ergot
<i>Fusarium</i> organisms	Grain	Deoxynivalenol
<i>Fusarium moniliforme</i>	Grain	Fumonisin
<i>Neotyphodium coenophialum</i>	Fescue	Ergovaline
<i>Penicillium</i> organisms	Grain	Aflatoxin
<i>Rhizoctonia leguminicola</i>	Legumes	Slaframine

Septicemia

An 18-year-old Morgan had a 10-day history of watery diarrhea, depression, and dysphagia. It died 4 days after being referred to a veterinary teaching hospital. *A. niger* was identified as the cause of vasculitis and brain infarction. *Mucor* and *Rhizopus* organisms were associated with a horse that developed myocarditis and nephritis after surgery.

Immunosuppression

Horses have occasionally developed systemic mold infections after corticosteroid treatment or natural immunosuppression. Fatal pulmonary infections with *A. flavus* and *A. niger* developed after corticosteroid immunosuppression or colic treatment. Two horses with myelomonocytic leukemia developed pulmonary aspergillosis. A chronic bronchopulmonary *Aspergillus* infection was diagnosed in a 30-year-old Saddlebred with Cushing's syndrome.

MOLD ALLERGIES

Heaves—also called *recurrent airway obstruction* (RAO), *chronic obstructive pulmonary disease* (COPD), “broken wind,” or “pulmonary emphysema” (see Chapter 8.4: “Heaves [Recurrent Airway Obstruction]: Practical Management of Acute Episodes and Prevention of Exacerbations”)—is a chronic inflammatory obstructive airway disease. Current evidence indicates that heaves is a delayed hypersensitivity response to inhaled antigens, particularly molds. Although horses with heaves have strong skin reactions after intradermal injections of mold extracts, more recent studies of dermal and pulmonary reactivities to *Micropolyspora faeni*, *A. fumigatus*, and *Thermoactinomyces*

vulgaris indicate that intradermal testing is of limited value in investigating heaves.

Studies of serum antibody titers have been equally disappointing. Circulating precipitins to *M. faeni* and *A. fumigatus* are not restricted to horses with heaves, although they do occur more frequently in this group.

The use of bronchoalveolar lavage fluid (BALF) has recently shed light on the pathogenesis of heaves. *M. faeni* and *A. fumigatus* have been identified as common causes of respiratory hypersensitivity in horses affected with heaves. An enzyme-linked immunosorbent assay (ELISA) was used to measure specific antibodies to *M. faeni* and to *A. fumigatus* in the serum and BALF of normal horses, horses with heaves, and horses with other respiratory diseases; elevated antibody results were not detected in the sera of any horses, but IgE and IgA antibodies to both allergens were significantly elevated in the BALF of heaves-affected horses. Horses with heaves have significantly higher concentrations of IgE and IgG directed to *A. fumi-*

gatus antigens in BALF even though they have no significant differences in serum.

Supplemental Readings

- Hess MB, Parker NA, Purswell BJ et al: Use of lufenuron as a treatment for fungal endometritis in four mares. *J Am Vet Med Assoc* 2002; 221:240, 266-267.
- Jackson CA, Berney C, Jefcoat AM et al: Environment and prednisone interactions in the treatment of recurrent airway obstruction (heaves). *Equine Vet J* 2000; 32:432-438.
- Lavoie JP, Maghni K, Desnoyers M et al: Neutrophilic airway inflammation in horses with heaves is characterized by a Th2-type cytokine profile. *Am J Respir Crit Care Med* 2001; 164:1410-1413.
- Leveille R, Hardy J, Robertson JT et al: Transarterial coil embolization of the internal and external carotid and maxillary arteries for prevention of hemorrhage from guttural pouch mycosis in horses. *Vet Surg* 2000; 29:389-397.
- Robinson NE, Derksen FJ, Olszewski MA et al: The pathogenesis of chronic obstructive pulmonary disease of horses. *Br Vet J* 1996; 152:283-306.

CHAPTER 15.9

Aflatoxicosis in Horses

STEPHEN B. HOOSER

West Lafayette, Indiana

Aflatoxins are mycotoxins that are produced by the fungi *Aspergillus flavus* and *Aspergillus parasiticus*. They are formed both while feeds are in storage and in the field. Aflatoxins are most commonly detected in corn, cottonseed, peanuts, and other sources of carbohydrates—usually grains. Formation of aflatoxins in feeds is related to environmental conditions such as relative humidity, temperature, and damage to the grains by insects or harvesting. Aflatoxin contamination of feeds more commonly occurs in the warm and humid conditions of the south and southeastern United States but can occur elsewhere under the appropriate conditions.

Although uncommon in horses, cases of aflatoxin poisoning have been reported in the United States and in other parts of the world. They are often associated with corn or peanuts. Whether the lack of reported cases is caused by use of higher quality feeds for horses or to lesser sensitivity of horses to their toxic effects is unknown. Among mammals, susceptibility to aflatoxins ranges from dogs (most sensitive) to young swine to calves to mature swine to mature cattle to sheep (least sensitive). From experimental studies, horses also appear to fall in the middle of the range of sensitivity, near mature cattle. In horses, single doses of 2 mg/kg of body weight have resulted in death within 76 hours of dosing. In feeding studies from the 1970s, daily consumption of aflatoxin in the feed at 0.075 mg/kg of body weight (roughly equivalent to 3800 parts per billion [ppb] per day in the feed) was seen to result in mortality at 37 to 39 days. At 0.3 mg/kg of body weight/day, death oc-

curred at 12 to 16 days after dosing began. As with other species, young horses and ponies seem to be more sensitive to the hepatotoxic effects of aflatoxin than are adults. Concentrations of aflatoxin in feed from reported clinical cases have ranged from 55 ppb to 6500 ppb. However, the concentrations of aflatoxin detected may not accurately reflect the amount actually ingested because concentrations of aflatoxin can vary widely within loads of grain and batches of feed. Therefore concentrations detected in any one sample may not be entirely representative of the whole.

After ingestion, aflatoxins are absorbed and metabolized to reactive epoxides—particularly in the liver but also in other tissues. These reactive epoxides bind to DNA and proteins, thus resulting in cell dysfunction and death. Because hepatocytes in the liver are the primary site of aflatoxin metabolism, these cells are severely affected. The major clinical signs associated with aflatoxin poisoning are related to liver damage and dysfunction. The degree of poisoning by aflatoxin follows a classic dose-response relationship. Ingestion of very large doses of aflatoxin results in massive liver damage with acute hepatic necrosis and possibly death within a few days, whereas ingestion of lesser amounts over a longer period of time results in more moderate hepatic injury that manifests as chronic liver failure.

CLINICAL SIGNS

Adverse clinical signs associated with aflatoxin poisoning are primarily related to severe, widespread liver damage.

vulgaris indicate that intradermal testing is of limited value in investigating heaves.

Studies of serum antibody titers have been equally disappointing. Circulating precipitins to *M. faeni* and *A. fumigatus* are not restricted to horses with heaves, although they do occur more frequently in this group.

The use of bronchoalveolar lavage fluid (BALF) has recently shed light on the pathogenesis of heaves. *M. faeni* and *A. fumigatus* have been identified as common causes of respiratory hypersensitivity in horses affected with heaves. An enzyme-linked immunosorbent assay (ELISA) was used to measure specific antibodies to *M. faeni* and to *A. fumigatus* in the serum and BALF of normal horses, horses with heaves, and horses with other respiratory diseases; elevated antibody results were not detected in the sera of any horses, but IgE and IgA antibodies to both allergens were significantly elevated in the BALF of heaves-affected horses. Horses with heaves have significantly higher concentrations of IgE and IgG directed to *A. fumi-*

gatus antigens in BALF even though they have no significant differences in serum.

Supplemental Readings

- Hess MB, Parker NA, Purswell BJ et al: Use of lufenuron as a treatment for fungal endometritis in four mares. *J Am Vet Med Assoc* 2002; 221:240, 266-267.
- Jackson CA, Berney C, Jefcoat AM et al: Environment and prednisone interactions in the treatment of recurrent airway obstruction (heaves). *Equine Vet J* 2000; 32:432-438.
- Lavoie JP, Maghni K, Desnoyers M et al: Neutrophilic airway inflammation in horses with heaves is characterized by a Th2-type cytokine profile. *Am J Respir Crit Care Med* 2001; 164:1410-1413.
- Leveille R, Hardy J, Robertson JT et al: Transarterial coil embolization of the internal and external carotid and maxillary arteries for prevention of hemorrhage from guttural pouch mycosis in horses. *Vet Surg* 2000; 29:389-397.
- Robinson NE, Derksen FJ, Olszewski MA et al: The pathogenesis of chronic obstructive pulmonary disease of horses. *Br Vet J* 1996; 152:283-306.

CHAPTER 15.9

Aflatoxicosis in Horses

STEPHEN B. HOOSER

West Lafayette, Indiana

Aflatoxins are mycotoxins that are produced by the fungi *Aspergillus flavus* and *Aspergillus parasiticus*. They are formed both while feeds are in storage and in the field. Aflatoxins are most commonly detected in corn, cottonseed, peanuts, and other sources of carbohydrates—usually grains. Formation of aflatoxins in feeds is related to environmental conditions such as relative humidity, temperature, and damage to the grains by insects or harvesting. Aflatoxin contamination of feeds more commonly occurs in the warm and humid conditions of the south and southeastern United States but can occur elsewhere under the appropriate conditions.

Although uncommon in horses, cases of aflatoxin poisoning have been reported in the United States and in other parts of the world. They are often associated with corn or peanuts. Whether the lack of reported cases is caused by use of higher quality feeds for horses or to lesser sensitivity of horses to their toxic effects is unknown. Among mammals, susceptibility to aflatoxins ranges from dogs (most sensitive) to young swine to calves to mature swine to mature cattle to sheep (least sensitive). From experimental studies, horses also appear to fall in the middle of the range of sensitivity, near mature cattle. In horses, single doses of 2 mg/kg of body weight have resulted in death within 76 hours of dosing. In feeding studies from the 1970s, daily consumption of aflatoxin in the feed at 0.075 mg/kg of body weight (roughly equivalent to 3800 parts per billion [ppb] per day in the feed) was seen to result in mortality at 37 to 39 days. At 0.3 mg/kg of body weight/day, death oc-

curred at 12 to 16 days after dosing began. As with other species, young horses and ponies seem to be more sensitive to the hepatotoxic effects of aflatoxin than are adults. Concentrations of aflatoxin in feed from reported clinical cases have ranged from 55 ppb to 6500 ppb. However, the concentrations of aflatoxin detected may not accurately reflect the amount actually ingested because concentrations of aflatoxin can vary widely within loads of grain and batches of feed. Therefore concentrations detected in any one sample may not be entirely representative of the whole.

After ingestion, aflatoxins are absorbed and metabolized to reactive epoxides—particularly in the liver but also in other tissues. These reactive epoxides bind to DNA and proteins, thus resulting in cell dysfunction and death. Because hepatocytes in the liver are the primary site of aflatoxin metabolism, these cells are severely affected. The major clinical signs associated with aflatoxin poisoning are related to liver damage and dysfunction. The degree of poisoning by aflatoxin follows a classic dose-response relationship. Ingestion of very large doses of aflatoxin results in massive liver damage with acute hepatic necrosis and possibly death within a few days, whereas ingestion of lesser amounts over a longer period of time results in more moderate hepatic injury that manifests as chronic liver failure.

CLINICAL SIGNS

Adverse clinical signs associated with aflatoxin poisoning are primarily related to severe, widespread liver damage.

In ponies given a single high dose of 2 mg/kg of body weight, clinical signs included anorexia, fever, tachycardia, ataxia, colic, icterus, bloody feces, tenesmus, and death. At a daily dose of 0.075 mg/kg of body weight, inappetence was noted at feeding day 13; more severe signs of depression, icterus, elevated temperature, tremors, and ataxia did not manifest until after day 32 of feeding (euthanasia at days 36 to 39).

DIAGNOSIS

A history of inappetence, weight loss, liver damage, and possibly hemorrhage that is associated with ingestion of feed containing grain, peanut meal, or cottonseed could be associated with aflatoxicosis. Chemical analysis of feed for aflatoxin is indicated. However, because clinical signs often appear weeks to months after ingestion (particularly after ingestion of low concentrations of toxin), feed analysis at the time adverse signs appear may not accurately reflect the feed that caused the liver damage. Because aflatoxins are rapidly metabolized, analysis of liver from affected animals is generally unrewarding unless the liver sample is obtained soon after the ingestion of large amounts of aflatoxin.

Serum biochemistry analyses reflect acute or chronic liver damage (see Chapter 3.26: "Liver Disease"). In particular, serum activities of sorbitol dehydrogenase and gamma-glutamyl transpeptidase may be elevated. In severe cases, prothrombin time may also be elevated and is associated with widespread hemorrhage. At necropsy, gross lesions associated with aflatoxicosis include icterus, hemorrhages, liver that is pale to yellow and firm, and intestinal hemorrhage. Microscopically, the primary lesions are in the liver and comprise hepatocyte necrosis, centrilobular fatty change, periportal fibrosis, and proliferation of bile ducts. Secondary renal tubular nephrosis is also sometimes noted.

In summary, the diagnosis of aflatoxicosis is based on

history, clinical signs, gross and microscopic lesions, and finding toxic amounts of aflatoxin in the feed. Because feed samples taken at the time adverse clinical signs appear may be negative, diagnosticians may be left with a history, clinical signs, and lesions that are suggestive of but not definitive for aflatoxicosis.

TREATMENT AND PREVENTION

No specific antidote exists for treating aflatoxicosis. Treatment is limited to supportive care for liver insufficiency. If hemorrhage is noted, vitamin K₁ therapy may be of benefit. Prevention of aflatoxicosis should emphasize the feeding of clean, high-quality grain that is stored under conditions of low moisture and is free of insects. If grain or feed is suspect, it should be tested for aflatoxins before feeding.

Supplemental Readings

- Aller WW, Edds GT, Asquith RL: Effects of aflatoxins in young ponies. *Am J Vet Res* 1981; 42:2162-2164.
- Angsubhakorn S, Poomvises P, Romruen K et al: Aflatoxicosis in horses. *J Am Vet Med Assoc* 1981; 178:274-278.
- Asquith RL, Edds GT, Aller WW et al: Plasma concentrations of iditol dehydrogenase (sorbitol dehydrogenase) in ponies treated with aflatoxin B₁. *Am J Vet Res* 1980; 41:925-927.
- Bortell R, Asquith RL, Edds GT et al: Acute experimentally induced aflatoxicosis in the weanling pony. *Am J Vet Res* 1983; 44:2110-2114.
- Cysewski SJ, Pier AC, Baetz AL et al: Experimental equine aflatoxicosis. *Toxicol Appl Pharmacol* 1982; 65:354-365.
- Osweiler GD, Carson TL, Buck WB et al: Mycotoxicoses. In Osweiler GD, Carson TL, Buck WB et al (eds): *Clinical and Diagnostic Veterinary Toxicology*, pp 409-442, Dubuque, Iowa, Kendall/Hunt Publishing, 1985.
- Vesonder R, Haliburton J, Stubblefield R et al: *Aspergillus flavus* and aflatoxins B₁, B₂, and M₁ in corn associated with equine death. *Arch Environ Contam Toxicol* 1991; 20:151-153.

CHAPTER 15.10

Ergopeptine Alkaloid Toxicoses in Horses

TIM J. EVANS
GEORGE E. ROTTINGHAUS
STAN W. CASTEEL
Columbia, Missouri

The large class of compounds known as *ergot alkaloids* primarily comprises the ergoline alkaloids (lysergic acid, lysergol, lysergic acid amide, and ergonovine) and the ergopeptine alkaloids (ergovaline, ergosine, ergotamine, ergocristine, ergocryptine, and ergocornine). Some debate regarding the relative roles of these different types of compounds in the etiology of animal toxicoses, especially in ruminants, exists. However, the ergopeptine alkaloids are the predominant toxins contained within fungal sclerotia found on ergotized grasses and cereal grains, and ergovaline is thought to be the most physiologically active ergot alkaloid produced by endophytic fungi in tall fescue. Unless otherwise specified, this chapter will focus on the diseases related to ergopeptine alkaloid exposure in horses. Concurrent exposure to other ergot alkaloids in endophyte-infected fescue and ergot bodies may also contribute to the production of clinical signs.

The fungal endophyte, *Neotyphodium coenophialum* (previously known as *Acremonium coenophialum* or *Epichloe typhina*), grows within the intercellular spaces of *Festuca arundinacea*, as part of a symbiotic, grass/endophyte relationship. The extremely vigorous Kentucky 31 cultivar of tall fescue grows on more than 35 million acres in the upper southeastern and lower midwestern regions of the United States. As part of its endophytic life cycle, *N. coenophialum* grows within the intercellular spaces and accumulates within the seed heads of tall fescue. Although also found in other parts of fescue grass, the ergopeptine alkaloid ergovaline is also found in highest concentrations in the seed heads.

Claviceps purpurea produces black, dark brown, or purple ergot bodies (sclerotia), which replace the individual seeds in the seed head of common pasture grasses—including fescues, bluegrasses, and brome-grasses—or cereal grains—such as oats, barley, wheat, and especially rye and triticale. The cool, wet springs in the northwestern United States and the northern Great Plains delay pollination and favor the germination and growth of *C. purpurea*. Ergot sclerotia resemble rodent droppings and vary in size, depending on the grass or grain infected by the fungus. Ergot bodies may be found within pastures, hays, grains, or processed feeds and concentrate within the screenings from ergotized grains. Ergotamine, ergocristine, ergosine, ergocornine, and ergocryptine are the primary ergopeptine alkaloids produced by *C. purpurea*.

MECHANISMS OF ACTION

Ergopeptine alkaloid/dopaminergic receptor interactions lead to vasoconstriction, suppression of prolactin secretion, and/or other physiologic effects. Vasoconstriction is associated with D₁-dopaminergic receptor inhibition and partial agonism of other receptor types, such as α_1 -adren-ergic and serotonin receptors. Stimulation of D₂-dopamine receptors by ergopeptine alkaloids decreases prolactin secretion by lactotropes located in the anterior pituitary. Lysergic acid amide, an ergoline alkaloid related to LSD, may cause sedation and other central nervous system effects in some animals. Stimulation of α_1 -adrenergic receptors in the myometrium by some ergot alkaloids has been associated with uterine contractions.

ERGOPEPTINE ALKALOID TOXICOSIS

Clinical Signs

Depending on the origin of the ergot alkaloid mycotoxins, toxicoses in horses produced by excessive exposure to ergopeptine alkaloids are best described as either equine fescue toxicosis or ergotism. These syndromes, which are indistinguishable from one another, may occur concurrently and are most commonly recognized in mares during late gestation and the early postpartum period. Clinical signs include agalactia, prolonged gestation, abortion, dystocia, and retained fetal membranes in mares. Preparturient signs—including normal udder development and “waxing”—are often absent, and foalings are often unanticipated and unsupervised. These unexpected parturitions in combination with oversized and dysmature foals predispose mares to dystocias and their sequelae. Fetal dysmaturity and mortality may be directly caused by ergopeptine alkaloids on fetal endocrine function or may be secondary to placental abnormalities, dystocia, and/or failure of passive transfer.

Increased incidences of laminitis and prolonged, post-exercise hyperthermia have also been reported in horses exposed to endophyte-infected fescue. In addition, delays in seasonal cycles, irregularities in estrous cycles, and increased occurrence of early embryonic death have all been reported in mares exposed to *N. coenophialum*. Given sufficient timing, duration, and level of exposure to the ergopeptine alkaloids in ergot sclerotia, similar clinical signs would be expected in equine ergotism. Gangrenous ergo-

tism and mortality have also been reported in association with exposure to high concentrations of ergopeptine alkaloids in ergotized grasses and cereal grains.

Diagnostic Testing

The detection of *N. coenophialum* in seeds or plant tissues or the presence of *C. purpurea* sclerotia in grasses or cereal grains suggests potential exposure to ergopeptine alkaloids. Because endophyte infection of tall fescue is not visibly distinguishable, a variety of analytic techniques have been described for the detection of endophyte in the stems, leaf sheaths, and/or seeds of tall fescue. Staining of plant samples with 0.5% solution of rose bengal in 5.0% aqueous ethanol or the use of ELISA methods or tissue-print immunoblotting techniques have been used to identify endophyte-infected fescue. Agricultural extension personnel or area agronomists should be consulted before sample collection to obtain specific sampling instructions. These individuals may also be helpful in the identification of ergotized grasses or grains.

The determination of ergopeptine alkaloid concentrations by enzyme-linked immunosorbent assay (ELISA) or high performance liquid chromatography (HPLC) does not confirm ingestion of ergopeptine alkaloids by livestock species, but it has the advantage over endophyte testing of detecting the toxic principles associated with fescue toxicosis and ergotism in grasses, hays, seeds or grains, and processed feeds. Endophyte-infected fescue has been reported to contain 200 to 600 $\mu\text{g/kg}$ (parts per billion [ppb]) of ergovaline. Clinical cases of agalactia in mares have been observed with ergovaline concentrations greater than 100 $\mu\text{g/kg}$ (ppb) in hay and with total ergopeptine alkaloid concentrations ranging from 500 to 1500 $\mu\text{g/kg}$ (ppb) in processed feeds that contain screenings of ergotized grain.

ELISA testing for urinary excretion of fescue ergot alkaloids has been used in cattle and is commercially available. Such analyses—if performed within 24 to 48 hours of animal removal from suspect pasture, hay, or grain-containing products—has provided a method of definitively confirming exposure to ergot alkaloids in cattle. Further research is being performed to determine the usefulness of this analytic technique in the confirmation of ergopeptine alkaloid exposure in horses.

Fescue toxicosis and ergotism are associated with alterations in circulating levels of several hormones. Significant decreases in plasma or serum levels of prolactin, progestins measured by radioimmunoassay, and relaxin (a sensitive indicator of placental function in the mare) have been noted in late-gestational mares (more than day 300 of gestation) exposed to ergopeptine alkaloids. The calcium concentrations of the mammary secretions present in agalactic mares seem to rarely exceed 50 ppm. Plasma levels of progestins measured by radioimmunoassay, cortisol, and triiodothyronine are decreased in the foals of mares that graze in endophyte-infected tall fescue pastures. Similar alterations would be expected in foals of mares exposed to ergot sclerotia.

Therapy

Successful treatment of fescue toxicosis and ergotism in horses depends on the early recognition of the clinical

signs and careful preparturient monitoring and assistance during foaling. If withdrawal of pregnant mares from endophyte-infected fescue and ergotized grasses or cereal grains is delayed until clinical signs of ergopeptine alkaloid toxicosis are apparent, treatment in addition to withdrawal may be indicated. The therapeutic efficacies of ergot alkaloid binders, increased dietary energy content, selenium supplementation, and phenothiazine administration have not been clearly demonstrated in pregnant mares that show signs of fescue toxicosis or ergotism. Dopamine- D_2 receptor antagonists, such as domperidone (1.1 mg/kg PO q24h), sulpiride (3.3 mg/kg PO q24h), perphenazine (0.3–0.5 mg/kg PO q12h), and acepromazine (20 mg/horse IM q6h) have all been reportedly used successfully in the treatment of agalactia in ergot alkaloid-exposed mares. The Rauwolfian alkaloid reserpine (2.0–5.0 mg/450 kg horse, q24h) depletes brain depots of dopamine, serotonin, and/or norepinephrine and appears to be effective for the treatment of postpartum agalactia in mares with a history of ergot alkaloid exposure. Domperidone has been demonstrated to be effective for the treatment of ergopeptine alkaloid-associated prolonged gestation in mares.

Perphenazine, unlike domperidone, crosses the blood-brain barrier in horses and has been associated with side effects, including excitability, hyperesthesia, and increased muscle tone. Diphenhydramine has been used to treat these adverse reactions. Excessive dripping of milk and the loss of colostral antibodies have been associated with the use of domperidone in mares, and prolonged sedation, diarrhea, and hypotension have been observed in some horses treated with reserpine. Dose adjustment, discontinuation of administration, and—in the case of domperidone—nasogastric intubation of foals with high-quality colostrum to prevent failure of passive transfer have been used to treat these adverse effects. Therapeutic or prophylactic use of domperidone in pregnant mares increases the calcium concentration in mammary secretions and renders the measurement of colostral calcium concentration unreliable as a predictor of impending parturition. Acepromazine is approved for use in the horse, and domperidone is approaching approval and commercial availability. Perphenazine and reserpine are human pharmacologic agents, and the recognized side effects of these drugs should also be taken into consideration before prescribing their use in mares affected by fescue toxicosis or ergotism.

Perphenazine has been used to advance seasonal cycles in pony mares exposed to ergopeptine alkaloids. The potential efficacies of domperidone and sulpiride for the stimulation of normal cyclic behavior in anestrus or transitional mares have been demonstrated in warmer environments, but some debate regarding the therapeutic value of these treatments in colder climates has arisen. Where low environmental temperatures are anticipated, withdrawal of broodmares from endophyte-infected fescue grass or hay or ergotized grasses or grains may be the treatment of choice for delayed seasonal cycles.

Prevention and Control

Recognition of the potential for exposure to the ergot alkaloid mycotoxins and an understanding of the risk factors predisposing animals to the development of clinical

signs of fescue toxicosis or ergotism are essential to the prevention and controls of these conditions. This is particularly true for pregnant mares, horses with chronic laminitis, and equine athletes. Knowledge of breeding dates, confirmation of pregnancy, careful monitoring of mammary gland development are critical in the identification of mares most susceptible to the effects of ergopeptine alkaloid exposure. Horses prone to laminitis should not be chronically exposed to ergopeptine alkaloids. For optimum performance, horses in athletic competition—especially in hot and humid climactic conditions—should have minimal exposure to ergot alkaloid mycotoxins.

Ergotism generally occurs sporadically, and exposure of pregnant mares to heavily ergotized feedstuffs can be avoided. Pastures, hays, and grains should be monitored for the presence of *C. purpurea* sclerotia, and the analysis of suspect forages or rations for ergopeptine alkaloid concentrations may be advisable. Crop rotation, deep cultivation, and the planting of nonergotized seed may reduce *C. purpurea* infection. Grain screenings should not be incorporated in feedstuffs intended for consumption by horses.

Avoidance of the use of toxigenic *N. coenophialum*-infected tall fescue in pastures or hays may be the best prophylactic approach to fescue toxicosis, but this may be more challenging than avoiding exposure to *C. purpurea* sclerotia. Complete pasture renovation and reseeding with endophyte-free fescue or other grass species is limited by the symbiotic nature of tall fescue grass/*Neotyphodium* interactions. Endophyte-free tall fescue is less adaptable and disease-resistant than fescue infected with *N. coenophialum*. Pastures of this less vigorous fescue grass will not flourish in many environments. The recent introduction of tall fescue infected with a genetically altered “friendly” endophyte has shown promise in preventing the clinical signs of fescue toxicosis in horses. This approach to fescue toxicosis prevention and control is limited by economic constraints, along with the possible, eventual reintroduction of “unfriendly” endophyte-infected fescue grass.

Strategic timing of withdrawal of horses from endophyte-infected pasture or hay may be the most practical prophylactic approach to equine fescue toxicosis. Periods as long as 60 to 90 days of withdrawal from tall fescue before anticipated foaling dates have been recommended for pregnant mares. However, the removal of pregnant mares from endophyte-infected pastures and the prevention of exposure to endophyte-infected hay 30 days before the expected foaling date (approximately day 300 of gestation) has generally been successful in controlling the incidence of equine fescue toxicosis. Ergopeptine alkaloid exposure may be best avoided in mares before the onset of normal cycles and the first 30 days of pregnancy, especially for individual mares with a history of subfertility.

Other pasture-management strategies may also play a role in the prevention and control of fescue toxicosis. Frequent mowing, heavy grazing pressure, and chemical

treatment to prevent or retard seed head development have been recommended as ways to decrease ergopeptine alkaloid concentrations in pastures. Dilution with at least 20% palatable legumes such as clovers has also been recommended in fescue pastures and may be a means of decreasing levels of ergopeptine alkaloids.

The use of a variety of binders to prevent the absorption of ergopeptine alkaloids has been advocated in horses and other livestock species to prevent fescue toxicosis and ergotism. However, the *in vivo* efficacy of these products remains questionable. Pharmacologic intervention has been used primarily in late-gestational mares to prevent the clinical signs of fescue toxicosis. This prophylactic approach may also be advisable in environments that favor the germination and growth of *C. purpurea* or when the risk of the incorporation of ergotized grains in the ration is increased. Medications used for this purpose at their therapeutic doses, beginning day 300 of gestation, include domperidone, sulpiride, and perphenazine. Another D₂-receptor antagonist, fluphenazine (25 mg IM in pony mares on day 320 of gestation) has also been recently advocated for the prevention of fescue toxicosis. Starting 10 to 14 days before the expected foaling date or on approximately day 330 of gestation—when mammary development is less than anticipated—domperidone has been used for the prevention of fescue toxicosis.

Supplemental Readings

- Brendemuehl JP: Reproductive aspects of fescue toxicosis. In Robinson NE (ed): Current Therapy in Equine Medicine, 4th edition, pp 571-573, Philadelphia, WB Saunders, 1997.
- Burrows GE, Tyrl RJ: Toxic Plants of North America, Ames, Iowa, Iowa State University Press, 2001.
- Cheeke PR: Natural Toxicants in Feeds, Forages, and Poisonous Plants, 2nd edition, Danville, Ill, Interstate Publishers, 1998.
- Cross DL, Redmond LM, Strickland JR: Equine fescue toxicosis: signs and solutions. J Anim Sci 1995; 73:899-908.
- Evans TJ, Rottinghaus GE, Casteel SW et al: Fescue toxicosis and ergotism. In Plumlee KH (ed): Clinical Veterinary Toxicology, St Louis, Mosby (in press).
- Green EM, Raisbeck MF: Fescue toxicosis. In Robinson NE (ed): Current Therapy in Equine Medicine, 4th edition, pp 670-673, Philadelphia, WB Saunders, 1997.
- Ireland FA, Loch WE, Worthy K et al: Effects of bromocriptine and perphenazine on prolactin and progesterone concentrations in pregnant mares during late gestation. J Reprod Fertil 1991; 92:179-186.
- Riet-Correa F, Mendez MC, Schild AL et al: Agalactia, reproductive problems and neonatal mortality in horses associated with ingestion of *Claviceps purpurea*. Aust Vet J 1988; 65:192-193.
- Ryan PL et al: Effects of exposing late-term pregnant mares to toxic and non-toxic endophyte-infected tall fescue pastures [abstract]. Biol Reprod 2001; 64(Suppl 1):612.
- Ryan PL, Bennett-Wimbush K, Vaala WE et al: Systemic relaxin in pregnant pony mares grazed on endophyte-infected fescue: effects of fluphenazine treatment. Theriogenology 2001; 56:471-483.

CHAPTER 15.11

Botulism

MATTHEW L. RENNINGER
STEPHEN B. HOOSER
West Lafayette, Indiana

Botulism is a neuromuscular disease characterized by flaccid paralysis that is caused by potent neurotoxins produced by strains of *Clostridium botulinum*. Botulism can affect mammals, birds, and fish; however, horses are one of the most susceptible species. It is sometimes called forage poisoning in adult horses and shaker foal syndrome in foals. Disease typically occurs in individual animals, but outbreaks occur.

ETIOLOGY AND PATHOGENESIS

C. botulinum are spore-producing, Gram-positive, anaerobic bacilli that thrive in decaying plant or animal tissue. Spores are found in the soil throughout much of the world. The distribution of strains of *C. botulinum* depends on environmental conditions, including temperature and soil pH. Strains of *C. botulinum* can produce one or more serotypes of neurotoxin and are named by the predominant toxin that they produce. Seven serotypes of botulinum neurotoxins exist and are labeled A, B, C₁, D, E, F, and G, all of which have similar toxicity. Type C₂ is not a neurotoxin but causes increased cellular permeability and diarrhea. In North America, botulism in horses is most often caused by type B toxin and less often by toxin types A and C₁.

Botulinum neurotoxins bind to presynaptic membranes at neuromuscular junctions, parasympathetic end plates, and cholinergic ganglia of the sympathetic nervous system and adrenal glands. These neurotoxins irreversibly block the release of the neurotransmitter acetylcholine, thus causing flaccid paralysis. Death often results from respiratory arrest. The central nervous system and sensory nerves are not affected.

Botulinum toxin can be absorbed from wounds infected with *C. botulinum* or from the gastrointestinal tract after ingestion of feed contaminated with the bacteria and/or preformed toxin. Toxin also can be both produced and absorbed in the gastrointestinal tract after ingestion of feed contaminated with spores that develop into bacteria that colonize the gut.

Botulism caused by bacterial infection of the gastrointestinal tract with subsequent toxin production is called toxicoinfectious botulism. Toxicoinfectious botulism typically occurs in foals; the normal flora of the gastrointestinal tract in adult animals prevents colonization of *C. botulinum*. The botulism bacteria are thought to colonize areas of necrosis, such as gastric ulcers. It has been suggested that grass sickness in adult horses can be caused by toxicoinfection with *C. botulinum* type C. Toxicoinfectious

botulism also can result from infection of the umbilicus or wounds, such as castration sites, that provide an anaerobic environment for infection.

Silage with a pH greater than 4.5 can be favorable for sporulation of *C. botulinum* and toxin production. Ingestion of spoiled silage or hay is typically associated with type B (and less often with type A) botulism. The resulting disease has been called "forage poisoning." Through examination of field cases it has also been suggested that birds may be able to carry preformed toxin from carrion to the feed of horses. This may be likely in part because of the extreme sensitivity of horses to the toxin compared to other species.

Ingestion of feed or water contaminated by the carcass of a rodent or other small animal is often associated with type C₁ botulism. In one outbreak alone, 38 horses on 17 different premises over a four-county area in southern California were affected with botulism through contamination of alfalfa cubes used as feed. Approximately 1000 horses were potentially exposed through feeding these alfalfa cubes. Because type C botulism was identified, the alfalfa was presumed to be contaminated with carrion. Of the 38 horses clinically affected, 31 (82%) died. Of ten horses treated with type C antitoxin and plasma from horses that had been vaccinated with type C toxoid, seven survived. Of six horses treated with type B toxoid, none survived.

CLINICAL SIGNS

The onset and rate of progression of clinical signs is directly related to the dose of botulinum toxin absorbed. Adverse signs may develop as early as a few hours or as late as 10 days after ingestion of toxin. These signs can range from mild to extremely severe and result in death within hours. Clinical signs are usually characterized by symmetric flaccid paralysis that is a result of irreversible blockade of acetylcholine release.

The initial adverse clinical signs in adult horses often include mild dysphagia with excessive salivation, exercise intolerance, weak eyelid tone, and weak tail tone. Horses may have noticeable difficulty swallowing and spend increased time attempting to eat and drink. They often develop generalized muscle weakness, tremors, carpal buckling, and ataxia, and they spend increased amounts of time resting. Muscle weakness can be mild to severe and progress to complete muscular paralysis and recumbency. Other clinical signs that may develop include mydriasis, vision deficits, ileus, constipation, and death.

Botulism in foals typically occurs at 2 to 5 weeks of age but can occur at any age. The initial clinical signs observed commonly include drooling while suckling and generalized weakness, which may be manifested as a slow stiff gait or increased time spent resting. Foals often develop muscle tremors, and the disease has been called shaker foal syndrome. They may become markedly weak and recumbent. Other clinical signs that may develop include tongue paralysis and dysphagia, mydriasis, weak eyelid tone, weak tail tone, ileus, and constipation.

Pharyngeal and lingual paralysis in adult horses and foals cause marked dysphagia and predispose them to aspiration pneumonia. Accumulation of gas from ileus can cause colic. Severely affected adult horses and foals may have an increased respiratory rate with decreased expansion of the chest due to paralysis of the diaphragm and intercostal muscles. Severely affected animals die from respiratory paralysis and cardiac failure.

DIAGNOSIS

Botulism should be suspected in horses with flaccid paralysis including the clinical signs described above or in horses found dead without other indications as to the cause of death. Botulinum toxin affects the cranial nerves but does not affect the central nervous system; thus a physical exam that demonstrates symmetric cranial nerve deficits in an animal with normal mentation can help set botulism apart from other differential diagnoses. Few or no changes are observed in the complete blood cell count and chemistry panel.

Botulism is often a clinical diagnosis. Definitive diagnosis of botulism is seldom achieved and is based on ruling out other causes. Detection of the toxin in soil, water, feed, serum, intestinal contents, or liver is possible using the mouse inoculation test. However, because horses are more sensitive to the effects of botulinum toxin than are mice, the toxin is often not demonstrated with this test. Botulinum toxin is more stable at cold temperatures, and serum samples for testing should be collected and frozen immediately after observation of clinical signs. If the toxin is demonstrated with mouse inoculation, the serotype can be determined through inoculation of mice passively protected with different serotypes of antitoxin. Detection of antibody titers in the serum of a recovering unvaccinated horse also provides evidence for diagnosis of botulism.

Observation of *C. botulinum* spores in the intestine of a horse with clinical signs supports a diagnosis of botulism but is not diagnostic. Although spores usually are not observed in horses without disease, spores can be ingested and observed as contaminants.

Differential diagnoses for botulism include viral causes of encephalitis (eastern and western equine encephalitis, rabies virus, equine herpesvirus 4, or West Nile virus; see Chapter 2.2: "Equine Herpesvirus" and Chapter 2.5: "Viral Encephalitides"), protozoal causes of encephalomyelitis (equine protozoal encephalomyelitis; see Chapter 2.11: "Equine Protozoal Myeloencephalitis"), and toxic causes of sudden death or neurologic dysfunction (organophosphate insecticides, lead, mycotoxins, yellow star thistle, *Centaurea solstitialis*; see Chapter 15.2: "Nigropallidal Encephalomalacia"), yew (*Taxus* sp.), or white snakeroot (*Eupatorium rugo-*

sum; see Chapter 15.3: "Plant-Induced Cardiac or Skeletal Muscle Necrosis"). Failure to demonstrate evidence of these pathogens and toxins supports a diagnosis of botulism.

Gross and microscopic lesions are typically not observed at necropsy unless related to secondary lesions such as aspiration pneumonia, decubital ulcers, or pressure myonecrosis.

TREATMENT AND PROGNOSIS

Botulism is usually fatal. In less severe cases, treatment can be successful if initiated soon after the onset of disease. Horses and foals should be immediately treated with a polyvalent antitoxin. Although antitoxin prevents botulinum toxin from binding to presynaptic membranes, the neurotoxin irreversibly blocks the release of acetylcholine, and antitoxin cannot reactivate affected neuromuscular junctions. The suggested dose of antitoxin is 200 ml for foals and 500 ml for adult horses. Generally, only one dose is needed and provides passive protection for up to 2 months. Evidence of recovery may not be observed for 4 to 10 days, and full recovery can take a month or more.

If toxicoinfectious botulism is suspected, antibiotics to eliminate *C. botulinum* may be administered. Antibiotics may also be given for treatment of secondary lesions, such as aspiration pneumonia or decubital ulcers. Aminoglycosides should be avoided because they are thought to possibly exacerbate clinical signs. Neurostimulants should not be used.

During recovery, affected animals should be confined to their stalls and kept calm and quiet. Soft thick bedding may help to prevent decubital ulcers in recumbent animals. Muzzling will help keep horses from attempting to eat their bedding and prevent aspiration pneumonia. Intense supportive therapy may be necessary and may include frequent turning of recumbent animals, nasogastric feeding and fluid support for animals with pharyngeal and lingual paralysis, frequent catheterization of the urinary bladder, and ventilatory support for animals with respiratory paralysis. Ophthalmic ointments should be used to protect the corneas.

Prognosis varies with the dose of toxin and severity of clinical signs. Mildly affected horses may recover with little treatment. Severely affected animals that become recumbent have a poor prognosis.

PREVENTION

Type B toxoid is available and should be used to prevent disease in areas in which type B botulism is endemic. According to the 1995 American Association of Equine Practitioners' vaccination guidelines, horses should be given an initial series of three vaccinations a month apart and then annual boosters. In pregnant mares, the booster should be given four weeks before parturition so the colostrum will contain adequate antibody to protect the foal. Foals can be vaccinated and will develop antibody even if they are passively protected. Unfortunately, type B vaccine only protects against exposure to type B toxin and does not provide cross-immunity for type C. Type C toxoid is not licensed for use in horses in North America.

Supplemental Readings

- American Association of Equine Practitioners' Subcommittee of the AVMA Council on Biologic and Therapeutic Agents: Guideline for vaccination of horses. *J Am Vet Med Assoc* 1995; 207:426-431.
- Galey FD: Botulism in the horse. *Vet Clin North Am* 2001; 17:579-589.
- Hunter LC, Poxton IR: Systemic antibodies to *Clostridium botulinum* type C: do they protect horses from grass sickness (dysautonomia)? *Equine Vet J* 2001; 33:547-553.
- Johnson EA, Bradshaw M: *Clostridium botulinum* and its neurotoxins: a metabolic and cellular perspective. *Toxicon* 2001; 39:1703-1722.

- Kinde H, Bettley RL, Ardans A et al: *Clostridium botulinum* type-C intoxication associated with consumption of processed alfalfa hay cubes in horses. *J Am Vet Med Assoc* 1991; 199:742-746.
- Rocke TL: *Clostridium botulinum*. In Gyles DL, Thoen CO (eds): *Pathogenesis of Bacterial Infections in Animals*, 2nd edition, pp 86-96, Ames, Iowa, Iowa State University Press, 1993.
- Schoenbaum MA, Hall SM, Glock RD et al: An outbreak of type C botulism in 12 horses and a mule. *J Am Vet Med Assoc* 2000; 217:365-368.

CHAPTER 15.12

Selenium Toxicity

MERL RAISBECK
Laramie, Wyoming

It has become *de rigueur* to begin any discussion of equine selenium (Se) poisoning with anecdotes of how the condition was responsible for Custer's loss at the Little Bighorn; however, little hard evidence exists that such was the case. In point of fact, even though Se was demonstrated to be toxic shortly after its discovery in the early 1800s, the first real identification of spontaneous selenium toxicity in domestic animals was the result of several years of painstaking investigations by the Experiment Stations at the Universities of South Dakota and Wyoming.

NATURAL HISTORY OF SELENIUM

Most of the Se in the geosphere occurs as metallic selenides in Cretaceous rocks and soils derived from these rocks. These highly reduced forms of Se (selenide or Se^{-2}) are insoluble in water and thus are not biologically available to plants or animals. However, when these ores are oxidized as a result of weathering, microbial action, or human activities such as mining, Se^{-2} is converted into more soluble and thus bioavailable selenite (SeO_3^{+4}) or selenate (SeO_4^{+4}). The latter ions are readily taken up by plants, incorporated into protein as selenomethionine (Semet) and thus become available to grazing animals.

Although all plant species can accumulate some (less than 40-50 ppm) Se in this fashion when grown on seleniferous soils, the so-called *accumulator species* also metabolize Se to volatile compounds that are readily eliminated and to nonphysiologic amino acids that are sequestered from the plant's metabolism. These mechanisms protect the plant from the toxic effects of Se and give it a significant competitive advantage over nonaccumulators in seleniferous soils. Bioconcentration from soil

Se may be as much as 10,000-fold, and plant tissue Se concentrations may reach 50,000 ppm. Accumulators are further divided into "facultative" (e.g., woody aster) which grow readily on both seleniferous and nonseleniferous soils and "obligate" accumulators (e.g., two-grooved milkvetch) which are only found in Se-rich soils. Although many texts attribute spontaneous selenosis to obligate accumulators, in fact these species are so unpalatable that most animals will starve before they eat any significant amount. Thus poisoning usually results from eating much larger amounts of normal forage species that contain much lower concentrations of the selenium.

On the other hand, most nutritional supplements consist of inorganic Se salts derived as byproducts during the refining of other minerals. Selenate and SeO_3^{+4} are cheaper than plant sources of Se and have good bioavailability but exhibit quite different toxicokinetics than so-called *natural* forms of Se. Because Se supplements start as highly purified salts rather than relatively low-concentration vegetation, considerable opportunity for miscalculation exists during the process of dilution of the supplements to physiologically useful concentrations that can be fed to horses. In this author's experience iatrogenic Se poisoning by Se supplements, either oral or parenteral, is much more common than naturally occurring selenosis.

PATHOPHYSIOLOGY

Several mechanisms have been postulated to explain the toxic effects of Se, which is chemically very similar to sulfur (S) and readily substitutes for S in many biochemical reactions. Se substitution in the disulfide bridges that provide tertiary structure and thus function to proteins is one

Supplemental Readings

- American Association of Equine Practitioners' Subcommittee of the AVMA Council on Biologic and Therapeutic Agents: Guideline for vaccination of horses. *J Am Vet Med Assoc* 1995; 207:426-431.
- Galey FD: Botulism in the horse. *Vet Clin North Am* 2001; 17:579-589.
- Hunter LC, Poxton IR: Systemic antibodies to *Clostridium botulinum* type C: do they protect horses from grass sickness (dysautonomia)? *Equine Vet J* 2001; 33:547-553.
- Johnson EA, Bradshaw M: *Clostridium botulinum* and its neurotoxins: a metabolic and cellular perspective. *Toxicon* 2001; 39:1703-1722.

- Kinde H, Bettel RL, Ardans A et al: *Clostridium botulinum* type-C intoxication associated with consumption of processed alfalfa hay cubes in horses. *J Am Vet Med Assoc* 1991; 199:742-746.
- Rocke TL: *Clostridium botulinum*. In Gyles DL, Thoen CO (eds): *Pathogenesis of Bacterial Infections in Animals*, 2nd edition, pp 86-96, Ames, Iowa, Iowa State University Press, 1993.
- Schoenbaum MA, Hall SM, Glock RD et al: An outbreak of type C botulism in 12 horses and a mule. *J Am Vet Med Assoc* 2000; 217:365-368.

CHAPTER 15.12

Selenium Toxicity

MERL RAISBECK
Laramie, Wyoming

It has become *de rigueur* to begin any discussion of equine selenium (Se) poisoning with anecdotes of how the condition was responsible for Custer's loss at the Little Bighorn; however, little hard evidence exists that such was the case. In point of fact, even though Se was demonstrated to be toxic shortly after its discovery in the early 1800s, the first real identification of spontaneous selenium toxicity in domestic animals was the result of several years of painstaking investigations by the Experiment Stations at the Universities of South Dakota and Wyoming.

NATURAL HISTORY OF SELENIUM

Most of the Se in the geosphere occurs as metallic selenides in Cretaceous rocks and soils derived from these rocks. These highly reduced forms of Se (selenide or Se^{-2}) are insoluble in water and thus are not biologically available to plants or animals. However, when these ores are oxidized as a result of weathering, microbial action, or human activities such as mining, Se^{-2} is converted into more soluble and thus bioavailable selenite (SeO_3^{+4}) or selenate (SeO_4^{+4}). The latter ions are readily taken up by plants, incorporated into protein as selenomethionine (Semet) and thus become available to grazing animals.

Although all plant species can accumulate some (less than 40-50 ppm) Se in this fashion when grown on seleniferous soils, the so-called *accumulator species* also metabolize Se to volatile compounds that are readily eliminated and to nonphysiologic amino acids that are sequestered from the plant's metabolism. These mechanisms protect the plant from the toxic effects of Se and give it a significant competitive advantage over nonaccumulators in seleniferous soils. Bioconcentration from soil

Se may be as much as 10,000-fold, and plant tissue Se concentrations may reach 50,000 ppm. Accumulators are further divided into "facultative" (e.g., woody aster) which grow readily on both seleniferous and nonseleniferous soils and "obligate" accumulators (e.g., two-grooved milkvetch) which are only found in Se-rich soils. Although many texts attribute spontaneous selenosis to obligate accumulators, in fact these species are so unpalatable that most animals will starve before they eat any significant amount. Thus poisoning usually results from eating much larger amounts of normal forage species that contain much lower concentrations of the selenium.

On the other hand, most nutritional supplements consist of inorganic Se salts derived as byproducts during the refining of other minerals. Selenate and SeO_3^{+4} are cheaper than plant sources of Se and have good bioavailability but exhibit quite different toxicokinetics than so-called *natural* forms of Se. Because Se supplements start as highly purified salts rather than relatively low-concentration vegetation, considerable opportunity for miscalculation exists during the process of dilution of the supplements to physiologically useful concentrations that can be fed to horses. In this author's experience iatrogenic Se poisoning by Se supplements, either oral or parenteral, is much more common than naturally occurring selenosis.

PATHOPHYSIOLOGY

Several mechanisms have been postulated to explain the toxic effects of Se, which is chemically very similar to sulfur (S) and readily substitutes for S in many biochemical reactions. Se substitution in the disulfide bridges that provide tertiary structure and thus function to proteins is one

of the earliest explanations for keratin abnormalities seen in selenosis. The selenite ion also reacts with reduced glutathione (GSH), which raises the possibility that the cytotoxic effects of Se result from denaturation of critical protein thiols.

Considerable evidence has recently accumulated for oxidative stress as the pivotal biochemical lesion of selenosis. Certain Se species react with tissue thiols to produce reactive oxygen species *in vitro*. Se intoxication is accompanied by numerous indices of oxidant damage *in vivo* and various antioxidant strategies lessen the impact of a given dosage of Se both *in vitro* and *in vivo*. Indirect evidence suggests that a relatively short-lived, highly reactive Se intermediate is responsible for this process *in vivo* but the specific molecule has not been conclusively identified.

The link between Se toxicity and oxidative stress is important given that Se is commonly described in the animal health literature as an *antioxidant* and many veterinarians and nutritionists seem to believe that one can compensate for a diet deficient in any antioxidant by feeding excess Se. Given the similarities between the lesions of vitamin E-Se deficiency and Se toxicity it behooves veterinarians to confirm a diagnosis of deficiency before instituting a supplementation program.

CLINICAL SIGNS

Acute Selenosis

This condition is almost always the result of overfeeding supplements or overdosing with parenteral preparations. Plants that accumulate enough Se to be acutely toxic are extremely unpalatable, and in numerous feeding experiments animals starved rather than eat them. Acute poisoning may present as sudden death with few, if any, clinical signs if the dose given was large enough. In most cases, however, signs of poisoning begin a few hours to a day or two after a toxic dose of Se. Clinical signs are generally referable to the gastrointestinal, cardiovascular, and respiratory systems.

Initially, intoxicated animals become lethargic and lose interest in feed. If the route of exposure was parenteral, the injection site will be sore. Poisoned animals often walk with a weak, wobbly gait. Careful clinical observation will reveal this ataxia to be the result of generalized weakness and shock rather than any specific neurologic deficit. Blindness is commonly described in many older texts; however, no well-documented cases exist of this sign in horses either experimentally or naturally unless some complicating factor is present (e.g., lead poisoning). Varying degrees of colic will be exhibited, especially if the route of exposure was oral. Excessive sweating is common. The affected animal's breath may have a "garlic" odor as a result of dimethyl selenide elimination. Watery, profuse diarrhea may occur, especially in animals that survive for longer periods of time.

Ventricular arrhythmias have been reported in experimentally poisoned animals and blood pressure reportedly drops even before clinical signs become apparent. Heart rate and respiration are elevated, but the pulse is weak and thready and peripheral circulation is compromised as evidenced by slow capillary refill and cold extremities. Dysp-

nea is prominent and poisoned animals may actually become cyanotic. Auscultation of the thorax reveals moist rales. Fever, polyuria, and hemolytic anemia have been reported but are not always present. Weakness progresses to prostration and coma with death resulting from circulatory and/or respiratory failure within a day or two of exposure.

The anorexia seen in acute selenosis is usually attributed to the general debility that accompanies poisoning. However, conditioned aversion to Se, that is, refusal to eat a feedstuff similar to one previously associated with a noxious stimulus, has been demonstrated in otherwise healthy birds, cattle, and antelope.

Poliomyelomalacia

Characterized by posterior paralysis or tetraparesis, poliomyelomalacia is a well-established effect of Se in swine and has been reported in one llama. However, no convincing reports exist of this condition in horses or other equidae.

Chronic Selenosis

Also known as *alkali disease*, chronic selenosis most frequently results from chronic (>30 days) consumption of seleniferous grains or forages, but may be (rarely) produced by shorter exposures or by sustained overfeeding of inorganic Se supplements. The characteristic signs of chronic selenosis are bilaterally symmetric alopecia and dystrophic hoof growth. Hair loss typically occurs along the nape of the neck and on the tail, but in severe cases other parts of the body may be affected.

The first signs of illness are transient lameness accompanied by erythema and swelling of the coronary bands. These early signs subside quickly and are easily missed if the horse is on pasture. The first signs are followed in 1 to a few days by development of a circumferential crack parallel to and just distal to the coronet (Figure 15.12-1). This crack results from defective tubular keratin produced by dermal papillae of the coronary band. Hoof separation and lameness progress together for several months until the damaged hoof is displaced from beneath by new growth and sloughs off. Affected animals are extremely lame and prolonged postural changes may result in damage to the appendicular skeleton. Without extensive nursing care, horses are unable to move to food or water and thus starve. Although no definitive experimental comparisons exist, it is this author's experience that the range of species susceptible to seleniferous vegetation or selenium, from most to least sensitive, is horses, cattle, and sheep.

Other spontaneous conditions that have been attributed to chronic selenosis include neurologic disease (so-called blind staggers), hemolytic anemia, and liver damage. Although anemia has been reported in rodents poisoned while on a semipurified diet, this is not a common finding in either experimental or field cases of poisoning in large animals. Few detailed studies exist of liver morphology and function in chronic selenosis. Early accounts that attribute severe hepatic damage to selenium are generally unreliable. Recent, well-designed studies report minimal, if any, morphologic changes in cattle, pigs,



Figure 15.12-1 Front hoof from horse with chronic selenosis (alkali disease). Horse was exposed to seleniferous (15 ppm) grass for approximately 30 days before becoming lame. Approximately 2 to 3 weeks after the onset of signs, lameness became so severe that the horse refused to stand to eat or drink and the owner opted for euthanasia. Note the beginning separation of the old keratin from the underlying new growth (arrow).

and sheep. One report exists, however, of clinicopathologic changes suggestive of liver disease in horses, and multifocal hepatic necrosis has been reported in cattle that died of acute selenosis.

Blind staggers (BS) is a neurologic condition that purportedly results from prolonged consumption of Se accumulators (especially *Astragalus* spp.) and presents as blindness, circling, head pressing, dysphagia, and paralysis in ruminants. Only two original reports exist of this condition in field cases, none in horses, and none from controlled experiments with either seleniferous plants or purified Se compounds, yet this rural legend continues to be repeated in texts and especially the horse-fancier literature. In fact, there is compelling evidence that BS is actually a potpourri of infectious, nutritional, and toxic diseases unrelated to Se (see O'Toole and colleagues in readings list).

Immunosuppression

Immunosuppression has been demonstrated after supranutritional but subclinically toxic doses of Se in waterfowl, rodents, cattle, and pronghorn antelope. The mechanism(s) is not understood but seems to involve antigen processing in the presence of high tissue Se concentrations. Although no direct experimental evidence exists in equidae, given the broad spectrum of species proven to be affected, similar effects in the horse can be reasonably expected.

DIAGNOSIS

The diagnosis of selenium intoxication rests on the traditional triad of clinical signs, biochemical and pathologic le-

sions, and chemical analysis. Sudden death, or sudden onset of lassitude, inappetence, diarrhea, pulmonary edema, cardiac arrhythmia, and shock after a change in feed should make an astute veterinarian consider the possibility of acute selenosis. Clinically normal herd-mates will exhibit severe aversion to the contaminated ration. Loss of mane and tail coupled with characteristic transverse hoof cracks several weeks or months after exposure to potentially seleniferous feedstuffs suggest chronic selenosis.

At *post mortem* examination myocardial necrosis may be grossly evident as pale streaks and hemorrhagic areas in the myocardium and accumulation of edema fluid in the lungs. Lungs may be edematous, emphysematous, or both. The bowel may be congested and hemorrhagic. In cattle and sheep, prolonged feeding of toxic amounts of inorganic Se salts produces histologic evidence of repeated episodes of myocardial necrosis and subsequent post-necrotic fibrosis similar to those of vitamin E-Se deficiency.

Keratinocytes, especially those that produce hard keratin, are the most characteristic target of chronic selenosis. Histologic examination of affected hoof and skin will reveal characteristic lesions including abnormal keratinocytes in the stratum spinosum or, in more severe cases, ballooning degeneration and necrosis of these same cells. Alopecia results from atrophy of primary hair follicles; secondary follicles are not affected. Affected hair follicles are collapsed and lack a hair shaft. The inner root sheath is atrophic or absent and the outer sheath contains dyskeratotic debris. Hoof changes are concentrated in a small area parallel to the coronary band. Dyskeratotic cells of the coronary papillae and the primary laminae produce debris that accumulates in horn tubules and distorts the normal architecture of the hoof wall.

Tissue Se concentrations are less predictive of tissue and organ damage than is the case with other toxicants such as lead (Pb). Specific concentrations vary with the tissue sampled, the chemical form of Se involved, and the type of analysis used. In general, inorganic Se typically used in supplements is cleared more rapidly than Se from "natural" sources such as forages and grains. Natural Se (specifically Semet) accumulates to greater concentrations in most tissues with chronic feeding yet appears to be less biologically available for either beneficial or toxic functions. Chemical analysis of Se in tissues is moderately difficult and "normal" or "toxic" ranges from one laboratory may not translate directly to results from another. With that caveat, the samples most commonly used for Se analysis are blood, serum, liver, kidney, hoof, and hair.

Serum Se concentrations increase quickly after a toxic dose but are fairly ephemeral and may return to normal range by the time an animal shows overt signs of chronic selenosis. Blood and liver concentrations are less prone to short-term fluctuations and remain elevated longer after a toxic dose. Concentrations greater than 1 ppm (as received basis) in any of these should raise at least the possibility of selenosis, especially after exposure to inorganic forms of Se. Under some conditions, however, considerably higher blood and liver concentrations may occur in clinically healthy animals, especially if the source of Se was forage. Some authors have suggested that the ratio of liver to kidney or plasma to albumin Se concentrations are definitive biomarkers of

selenium intoxication. This theory has not been tested in horses, however, and is not completely reliable in livestock.

Theoretically, once Se is deposited in keratinized tissues such as hoof and hair it is metabolically inert and thus is a reliable long-term indicator of Se intake. In horses on Se-adequate diets hair Se concentrations usually range from slightly less than 1 ppm to slightly more than 1 ppm. Concentrations greater than 5 ppm are indicative of excessive Se exposure and presumably selenosis. Some caution in interpretation is warranted, because Se is elevated only in hair and hoof that was produced while blood concentrations were elevated. It is not unusual to see a 10-fold or greater variation in Se concentration along a hair shaft or between different parts of a hoof. Used judiciously, this fact can be used to approximate the temporal pattern of Se exposure; segments closer to the skin represent more recent exposure. It is important, however, to sample hair that was actively growing during the period of exposure—usually the mane and tail.

PREVENTION, MANAGEMENT, AND THERAPY

No proven specific therapy exists for acute Se intoxication. Symptomatic and supportive therapy may be useful in some cases, but the prognosis for any animal afflicted with acute selenosis is poor. Experimentally, massive doses of vitamin E ameliorate many of the cytotoxic effects of Se in laboratory animals and birds if given before or soon after intoxication. This strategy has not been tested in horses but, on the basis of rodent and avian studies, it would require 10 to 20 times a normal therapeutic dose. Experimentally, sulfobromophthalein enhances biliary excretion and decreases urinary excretion of ^{75}Se -selenite in rats by scavenging reactive Se metabolites in tissues before they can attack cellular components. Again, this regimen has not been tested in horses or other large mammals.

Uncomplicated chronic selenosis in horses can be successfully treated with low Se, high-protein, high-quality diets, and supportive care. The nursing care required is quite extensive, however, and owners should be warned about the effort required to care for an invalid for 2 to 4 months. Horses should be provided soft, sandy footing to lessen the pain associated with standing and walking. Nonsteroidal antiinflammatory agents, heart-bar shoes, and even analgesics may be used to permit affected animals some movement and to maintain normal food and water intake. Frequent therapeutic hoof trimming should

be used to minimize abnormal posture and resultant secondary joint and skeletal problems.

Prevention consists of avoidance of excessive dietary or parenteral Se. Se, like many essential trace elements, has a very narrow safety margin and poisoning may easily result from miscalculations in dose. Total dietary Se concentrations as low as 5 ppm (dry matter) may, under some circumstances, be toxic. Dietary imbalances such as low protein or vitamin E increase susceptibility to Se toxicity. A diet deficient in Se itself predisposes animals to selenosis.

In seleniferous areas it may be impossible to completely avoid excess dietary Se, yet strategies exist to minimize poisoning. Selenium concentrations in edible forage grasses peak between heading and maturity. Although the precise timing of peak concentrations may differ between regions and with different forage mixtures, it is consistent for any given locale. Using known seleniferous pastures before or after this critical period lessens the exposure to Se. Seleniferous vegetation in large pastures is often concentrated in "hot spots" where plant concentrations may be 2 to 10 times greater than the rest of the pasture. Identification of these areas by forage sampling and fencing them out may lower total dietary intake below toxic thresholds.

Experimentally, the administration of arsenic compounds such as arsanilic acid has lessened the severity of selenosis, especially in swine. This approach has not, however, proved very beneficial under field conditions with natural cases of selenosis. Linseed oil meal protects rats and chickens against some of the effects of chronic selenosis, but again, the practice has not lived up to its promise under field conditions.

Supplemental Readings

- O'Toole D, Raisbeck MF: Magic numbers, elusive lesions: comparative aspects of selenium toxicosis in herbivores and waterfowl. In Frankenberger WT, Engberg RA (eds): *Environmental Chemistry of Selenium*, pp 355-395, London, Marcel Dekker, 1997.
- O'Toole D, Raisbeck MF, Case JC et al: Selenium-induced "blind staggers" and related myths: a commentary on the extent of historical livestock losses attributed to selenosis in the western U.S. rangelands. *Vet Pathol* 1996; 33:109-116.
- Raisbeck MF, Dahl ER, Sanchez DA et al: Naturally occurring selenosis in Wyoming. *J Vet Diagn Invest* 1993; 5:84-87.
- Raisbeck MF, O'Toole D: Morphologic studies of chronic selenosis in herbivores. In Garland T, Barr AC (eds): *Toxic Plants and Other Natural Toxicants*, pp 380-389, Wallingford, United Kingdom, CAB International, 1998.

SECTION XVI

Endocrine Disorders

Edited by Dr. Phillip J. Johnson

CHAPTER 16.1

Thyroid Dysfunction

NATHANIEL T. MESSER IV
Columbia, Missouri

TYPES OF THYROID DYSFUNCTION

Disorders of thyroid gland function in horses are uncommon, not well documented, and in most cases incompletely understood. Hypothyroidism accounts for most cases described in horses. Hypothyroidism is indicated by low serum levels of biologically active thyroid hormones and is classified as primary, secondary, or tertiary, depending on the cause. Primary hypothyroidism, caused by intrinsic thyroid gland disease, is very rare in horses. Secondary hypothyroidism, caused by inadequate production and/or release of thyrotropin (TSH), may be the most common form of hypothyroidism in horses, but is difficult to diagnose because of the lack of specific equine TSH assays. Tertiary hypothyroidism, caused by inadequate production and/or release of thyrotropin-releasing hormone (TRH) has not been described in horses and would be difficult to differentiate from secondary hypothyroidism without specific assays for either TSH or TRH.

A congenital form of primary hypothyroidism has been described in foals in Canada and in the northern tier of states in the United States. In this form foals are born with thyroid dysfunction, thyroid gland hyperplasia, and various developmental musculoskeletal abnormalities potentially caused by a combination of high nitrate levels and low levels of iodine in the feed of pregnant mares in that region. Hyperthyroidism, characterized by high serum levels of biologically active thyroid hormones, has recently been described in association with thyroid gland neoplasia.

A number of nonthyroidal factors may affect serum levels of thyroid hormones in horses with normal thyroid glands (i.e., euthyroid horses). These factors exert their effects through disruption of the normal pituitary-thyroid axis or by affecting peripheral thyroid hormone action or metabolism. The effect of phenylbutazone on serum levels of thyroid hormone is a good example. Because phenylbutazone is highly protein bound it tends to displace thyroid

hormones from protein binding sites, effectively increasing levels of free hormone which then decrease TSH release through negative feedback. This process results in decreased production of thyroid hormones by the thyroid gland. Other nonthyroidal factors shown to cause low serum levels of thyroid hormones in horses with essentially normal thyroid glands include high-energy diets, high-protein diets, food deprivation, level of training, stage of pregnancy, diets high in zinc and copper, diets high in iodine, diets with a high carbohydrate:roughage ratio, conditions associated with glucocorticoid excess, and ingestion of endophyte-infected fescue grass. Other as yet unidentified factors no doubt exist that could potentially affect thyroid hormone levels in euthyroid horses.

CLINICAL SIGNS

A variety of clinical signs and conditions have been attributed to low serum levels of thyroid hormones in horses. Such conditions as obesity, "cresty" necks, laminitis, and infertility have all been attributed to low levels of thyroid hormones in clinical practice. However, the clinical signs that result from surgical thyroidectomy, in which serum levels of thyroid hormone are typically undetectable, are considerably different than those usually associated with "hypothyroidism" in clinical practice. Thyroidectomized horses are more sensitive to cold temperatures, have coarse hair coats, mild alopecia, delayed shedding of hair coat, thickened facial features, edema in the hind legs, decreased feed consumption, decreased weight gains, lower rectal temperature, lower heart rate, decreased cardiac output, and exercise intolerance. Thyroidectomized mares continue to cycle, become pregnant, and subsequently deliver normal foals. Thyroidectomized stallions show reduced libido but their fertility is normal.

A possible explanation for this discrepancy is that low serum levels of thyroid hormones occur as a result of an-

other disease process or endocrine abnormality and are inappropriately attributed to thyroid gland dysfunction. The underlying disease or abnormality is actually the cause of the clinical signs observed and not the low thyroid hormone levels. Many of the clinical signs associated with low serum levels of thyroid hormones in clinical practice are nonspecific and have been shown to occur in horses with other diseases or endocrine abnormalities.

The congenital form of hypothyroidism described in foals born in western Canada and the Pacific Northwest is characterized by thyroid gland hyperplasia and various musculoskeletal deformities. These foals show signs of dysmaturity and incomplete skeletal development including angular limb deformities, mandibular prognathism, and incomplete ossification of cuboidal bones of the carpus and tarsus. Other abnormalities include anemia, hyperlipemia, low rectal temperatures, and dry hair coats. Many foals die as a result of this condition, and those that survive have ongoing musculoskeletal disease that is unresponsive to thyroid hormone supplementation.

In cases of reported hyperthyroidism associated with thyroid gland neoplasia in which high serum levels of thyroid hormones were present, clinical signs similar to those seen in other species were present including weight loss, hyperexcitability, tachycardia, polyphagia, and enlargement of the thyroid gland. These clinical signs disappeared after removal of the tumor.

EVALUATION OF THYROID DYSFUNCTION

Most cases of hypothyroidism are inappropriately diagnosed based on clinical signs, measurement of serum levels of thyroid hormones (total triiodothyronine [T3] and thyroxine [T4]), and response to therapy with thyroid hormone supplementation. As discussed previously, clinical signs frequently associated with hypothyroidism have not been recognized in thyroidectomized horses, thus clinical signs other than those seen in thyroidectomized horses may not be reliable diagnostic criteria. Serum thyroid hormone levels when used alone are insensitive and often misleading, which frequently results in the misdiagnosis of hypothyroidism in horses. Measurement of free forms of thyroid hormones does reflect levels of biologically active thyroid hormones but in horses does not appear to provide additional useful information for the assessment of thyroid dysfunction. A favorable response to therapy with thyroid hormone supplement is commonly cited as evidence of hypothyroidism, but because thyroid hormone supplementation improves overall metabolism, it may help horses affected with a variety of nonthyroidal illnesses and in addition may not be indicative of hypothyroidism.

Accurate diagnosis of hypothyroidism must depend on the use of additional diagnostic tests to determine if the function of the hypothalamic-pituitary-thyroid axis is normal. Horses with a normal hypothalamic-pituitary-thyroid axis should not be referred to as *hypothyroid*. Ideally, the use of specific equine TSH assays combined with either TSH- or TRH-stimulation tests are required to accurately differentiate primary from secondary hypothyroidism and to differentiate both from other conditions that result in low serum thyroid hormone levels in otherwise euthyroid

horses. Unfortunately these additional tests are used less frequently in horses because of their expense, limited availability, safety issues, and the potential for spurious results. Validated assays for equine TSH are not yet readily available for routine testing. Commercially available TSH and TRH for injection are both expensive and occasionally unavailable. Reagent-grade TRH is being used for diagnostic testing in research applications and for clinical use by some veterinarians. This variety of TRH is not packaged for sterile injection, however, and should thus be used with caution. In forms of secondary hypothyroidism in which abnormal TSH release or TRH-induced TSH release is present as might occur in states of glucocorticoid excess or during long-term supplementation with exogenous thyroid hormone, a minimal response to TRH stimulation may occur and result in the misdiagnosis of primary hypothyroidism.

The TRH stimulation test is currently the only means to evaluate the status of the hypothalamic-pituitary-thyroid axis. To perform this test, the clinician should collect a serum sample just before testing, administer 1 mg of TRH intravenously and then collect serum samples 2 and 4 hours after administration of TRH. Serum levels of T3 and T4 in normal horses will be at least twice that of baseline after 2 and 4 hours, respectively. This test will not distinguish primary hypothyroidism from other forms of hypothyroidism and does have the limitations mentioned previously in this chapter. Because validated assays for equine TSH are not yet readily available for routine testing, naturally occurring thyroid dysfunction in adult horses remains difficult to characterize.

TREATMENT

Thyroid hormone supplementation should be implemented when horses have clinical signs similar to those observed in thyroidectomized horses—persistently low serum levels of thyroid hormones, and an inadequate response to TRH stimulation testing (known nonthyroidal factors that affect thyroid function, mentioned previously in this chapter, should have been ruled out as an underlying cause). Thyroid hormone supplementation in horses that have low serum levels of thyroid hormones caused by conditions other than primary hypothyroidism has unknown benefit and may in some instances be detrimental.

A number of thyroid hormone replacement therapies are commercially available for use in horses. Treatment protocols should follow the label recommendation of the manufacturer and be accompanied by regular measurement of serum thyroid hormone levels to evaluate the effectiveness of the treatment.

In cases of hyperthyroidism associated with thyroid gland neoplasia, surgical removal of the thyroid tumor resulted in a return to normal thyroid hormone levels.

Supplemental Readings

Allen AL, Doige CE, Fretz PB et al: Hyperplasia of the thyroid gland and concurrent musculoskeletal deformities in western Canadian foals—reexamination of a previously described syndrome. *Can Vet J* 1994; 35:31-38.

Beech J: Disorders of thyroid gland function. In Watson TDG (ed): Metabolic and Endocrine Problems of the Horse, pp 69-74, Philadelphia, WB Saunders, 1998.

Breuhäus BA: Thyroid-stimulating hormone in adult euthyroid and hypothyroid horses. J Vet Intern Med 2002; 16:109-115.

Frank N, Sojka J, Messer NT: Equine thyroid dysfunction. Vet Clin North Am Equine Pract (in press).

Messer NT: Thyroid disease (dysfunction). In Robinson NE (ed): Current Therapy in Equine Medicine, ed 4, pp 502-503, Philadelphia, WB Saunders, 1997.

Messer NT, Riddle WT, Traub-Dargatz JL et al: Thyroid hormone levels in Thoroughbred mares and their foals at parturition. Proceedings of the 44th Annual Meeting of the American Association of Equine Practitioners, pp 248-251, 1998.

Mooney CT, Murphy D: Equine hypothyroidism—the difficulties of diagnosis. Equine Vet Educ 1995; 7:242-245.

Sojka JE: Hypothyroidism in horses. Comp Cont Educ Pract Vet 1995; 17:845-852.

CHAPTER 16.2

Pituitary *Pars Intermedia* Dysfunction: Equine Cushing's Disease

HAROLD C. SCHOTT II
East Lansing, Michigan

Over the past decade diagnostic evaluation and treatment of horses with pituitary *pars intermedia* dysfunction—more commonly known as equine Cushing's disease—has increased dramatically, largely because clients want to maintain their horses in the best possible health through their third and even fourth decades.

In humans, Cushing's disease is most commonly attributed to a corticotroph adenoma in the *pars distalis* of the pituitary gland. In contrast, Cushing's disease in horses is almost exclusively attributed to hyperplasia or adenoma formation in the *pars intermedia* of the pituitary. Abnormal *pars intermedia* cells produce excessive amounts of pro-opiomelanocortin (POMC) and a number of POMC-derived peptides in addition to adrenocorticotrophic hormone (ACTH). These differences in location and function between human and equine pituitary adenomas have lead several authors to suggest that the disease in horses should not be called equine Cushing's disease; rather, pituitary *pars intermedia* dysfunction (PPID) has been advanced as a more appropriate descriptor. In a pathology study of pituitary glands collected from 19 horses with PPID, 13 (68%) had *pars intermedia* macroadenomas (>1 cm in diameter) that replaced most of the *pars distalis*, and six horses (32%) had microadenomas. The adenomas were sharply delineated from surrounding tissue but did not have definite capsules. The tumors caused varying degrees of compression of the *pars distalis* and occasionally infiltrated—or even ablated—the neurohypophysis. Dorsal expansion of the tumor through the diaphragma sella can lead to compression of the hypothalamus and optic chiasm, thus resulting in blindness and other neurologic deficits. *Pars intermedia* adenoma cells have a low mitotic

index and have not been reported to metastasize. Adrenocortical hyperplasia accompanying PPID is relatively uncommon, occurring in about 20% of affected horses.

One of the more interesting—and as yet unanswered—questions about PPID in horses is whether it is a spontaneous pituitary disease or is a consequence of loss of dopaminergic innervation and thereby a primary hypothalamic disorder. Although adenomas of the *pars distalis* in humans with Cushing's disease are thought to arise spontaneously, *pars intermedia* hyperplasia in horses with PPID resembles that resulting from denervation of the *pars intermedia* in rats or that observed during growth in cell culture. *Pars intermedia* tumors in horses contain markedly reduced amounts of dopamine—about 10% that of normal *pars intermedia* tissue—consistent with a specific loss of hypothalamic dopaminergic innervation. Further, loss of a specific population of dopaminergic neurons is seen with other disorders, including yellow star thistle toxicosis in horses and Parkinson's disease in humans. Taken together, these findings could support primary hypothalamic disease, but they could also result from adenomatous cells that outgrow their innervation. Thus whether PPID in horses is a consequence of specific loss of dopaminergic neurons (primary hypothalamic disease) or arises spontaneously (primary pituitary disease) is unclear.

CLINICAL SIGNS

Although the frequency of diagnosis and treatment of PPID in horses has clearly increased over the past decade, no evidence suggests that the prevalence of PPID

Beech J: Disorders of thyroid gland function. In Watson TDG (ed): Metabolic and Endocrine Problems of the Horse, pp 69-74, Philadelphia, WB Saunders, 1998.

Breuhäus BA: Thyroid-stimulating hormone in adult euthyroid and hypothyroid horses. J Vet Intern Med 2002; 16:109-115.

Frank N, Sojka J, Messer NT: Equine thyroid dysfunction. Vet Clin North Am Equine Pract (in press).

Messer NT: Thyroid disease (dysfunction). In Robinson NE (ed): Current Therapy in Equine Medicine, ed 4, pp 502-503, Philadelphia, WB Saunders, 1997.

Messer NT, Riddle WT, Traub-Dargatz JL et al: Thyroid hormone levels in Thoroughbred mares and their foals at parturition. Proceedings of the 44th Annual Meeting of the American Association of Equine Practitioners, pp 248-251, 1998.

Mooney CT, Murphy D: Equine hypothyroidism—the difficulties of diagnosis. Equine Vet Educ 1995; 7:242-245.

Sojka JE: Hypothyroidism in horses. Comp Cont Educ Pract Vet 1995; 17:845-852.

CHAPTER 16.2

Pituitary *Pars Intermedia* Dysfunction: Equine Cushing's Disease

HAROLD C. SCHOTT II
East Lansing, Michigan

Over the past decade diagnostic evaluation and treatment of horses with pituitary *pars intermedia* dysfunction—more commonly known as equine Cushing's disease—has increased dramatically, largely because clients want to maintain their horses in the best possible health through their third and even fourth decades.

In humans, Cushing's disease is most commonly attributed to a corticotroph adenoma in the *pars distalis* of the pituitary gland. In contrast, Cushing's disease in horses is almost exclusively attributed to hyperplasia or adenoma formation in the *pars intermedia* of the pituitary. Abnormal *pars intermedia* cells produce excessive amounts of pro-opiomelanocortin (POMC) and a number of POMC-derived peptides in addition to adrenocorticotrophic hormone (ACTH). These differences in location and function between human and equine pituitary adenomas have lead several authors to suggest that the disease in horses should not be called equine Cushing's disease; rather, pituitary *pars intermedia* dysfunction (PPID) has been advanced as a more appropriate descriptor. In a pathology study of pituitary glands collected from 19 horses with PPID, 13 (68%) had *pars intermedia* macroadenomas (>1 cm in diameter) that replaced most of the *pars distalis*, and six horses (32%) had microadenomas. The adenomas were sharply delineated from surrounding tissue but did not have definite capsules. The tumors caused varying degrees of compression of the *pars distalis* and occasionally infiltrated—or even ablated—the neurohypophysis. Dorsal expansion of the tumor through the diaphragma sella can lead to compression of the hypothalamus and optic chiasm, thus resulting in blindness and other neurologic deficits. *Pars intermedia* adenoma cells have a low mitotic

index and have not been reported to metastasize. Adrenocortical hyperplasia accompanying PPID is relatively uncommon, occurring in about 20% of affected horses.

One of the more interesting—and as yet unanswered—questions about PPID in horses is whether it is a spontaneous pituitary disease or is a consequence of loss of dopaminergic innervation and thereby a primary hypothalamic disorder. Although adenomas of the *pars distalis* in humans with Cushing's disease are thought to arise spontaneously, *pars intermedia* hyperplasia in horses with PPID resembles that resulting from denervation of the *pars intermedia* in rats or that observed during growth in cell culture. *Pars intermedia* tumors in horses contain markedly reduced amounts of dopamine—about 10% that of normal *pars intermedia* tissue—consistent with a specific loss of hypothalamic dopaminergic innervation. Further, loss of a specific population of dopaminergic neurons is seen with other disorders, including yellow star thistle toxicosis in horses and Parkinson's disease in humans. Taken together, these findings could support primary hypothalamic disease, but they could also result from adenomatous cells that outgrow their innervation. Thus whether PPID in horses is a consequence of specific loss of dopaminergic neurons (primary hypothalamic disease) or arises spontaneously (primary pituitary disease) is unclear.

CLINICAL SIGNS

Although the frequency of diagnosis and treatment of PPID in horses has clearly increased over the past decade, no evidence suggests that the prevalence of PPID

is actually increasing. Increased recognition of the disease is likely a consequence of clients maintaining their horses to more advanced ages as well as increased health care being provided to older horses. All breeds and types of equidae can be affected with PPID, but ponies and Morgan horses appear to be at greater risk. No gender predilection exists. The mean age of affected horses is generally 18 to 23 years, but cases have been reported in mares as young as 7 years.

The classic clinical sign of PPID in horses is hirsutism, a long and curly hair coat that fails to shed. During the initial months to years of PPID, long hair growth may be restricted to the lower jaw, base of the neck, and the palmar and plantar aspects of the distal limbs. Over time, generalized hirsutism may develop, and occasionally a dark hair coat may turn lighter in color. The pathogenesis of this peculiar clinical sign, which is characterized by arrest of hair follicles in telogen, remains unknown. It has been suggested that hirsutism is a consequence of chronic elevations in POMC peptides, specifically melanocyte-stimulating hormone. Hyperhidrosis is also observed in up to two thirds of horses with PPID—most commonly over the neck and shoulders—and has been attributed to a thermoregulatory response to the long hair coat.

Weight loss and lethargy, or poor performance, are also commonly observed in horses with PPID. In addition to true weight loss, protein catabolism caused by increased cortisol activity leads to loss of muscle mass. This is most notable in advanced cases as a loss of epaxial and rump musculature. Owners may not recognize muscle wasting until it is moderate to advanced because weakness and stretching of the abdominal muscles often maintains the “roundness” of the abdomen. Despite weight loss, appetite in affected horses is normal or even increased. However, dental abnormalities that lead to painful mastication and quidding may compromise feed intake and contribute to weight loss in some horses. Combined with—or often preceding—loss of muscle mass is deposition of fat along the crest of the neck, over the tail head, and in the sheath of male horses. Another area where abnormal fat deposition may occur is above and behind the eyes (supraorbital area). Lethargy and poor performance are expected findings with most chronic diseases. However, horses with PPID have also been described as overly docile and more tolerant of pain than normal horses. The latter signs have been attributed to increased plasma and cerebrospinal fluid concentrations of β -endorphin that are sixtyfold and more than 100-fold greater, respectively, in horses with PPID than in normal horses.

Chronic, insidious-onset laminitis is perhaps the major clinical complication of PPID; more than 50% of horses are affected in most reports. Although the condition is more amenable to management in ponies because of their lighter body weight, chronic or recurrent pain with exacerbation of laminitis or associated foot abscesses is often the reason for euthanasia.

Polyuria and polydipsia (PU/PD) has been described in approximately one-third of horses with PPID. Mechanisms leading to PU/PD in horses with PPID may include osmotic diuresis (with hyperglycemia and glucosuria), development of partial neurogenic diabetes insipidus caused by destruction of the neurohypophysis by expansion of

the *pars intermedia*, and central stimulation of thirst by hypercortisolism. In general, PU/PD in horses with PPID is usually modest and is rarely of clinical significance. A potential urinary tract complication in horses and other species with hypercortisolism is urinary tract infection. Urinary tract infection may lead to dysuria or may be silent.

Equids with PPID tend to have delayed wound healing and often are affected with secondary infections. Commonly recognized infections include skin infections (e.g., refractory “scratches” and fistulous tracts), recurrent sub-solar abscesses, conjunctivitis, sinusitis, gingivitis, alveolar periostitis, and bronchopneumonia, which is often a mixed bacterial and fungal infection. Other clinical signs that have been reported in horses with PPID include persistent lactation and infertility—probably a consequence of altered release of prolactin and gonadotrophic hormones. Signs of central nervous system (CNS) dysfunction—including ataxia, blindness, and seizures—are occasionally observed in equids with PPID. Although blindness is typically thought to be a consequence of compression of the optic chiasm by the pituitary tumor, no relationship has been found between tumor size and several clinical signs (laminitis, blindness, and seizures) or plasma concentrations of ACTH, cortisol, glucose, or insulin.

A major complication of hypercortisolism in affected human patients is osteoporosis. Although occurrence of this complication has not been investigated in horses, it is interesting to note that euthanasia of horses with PPID is often performed after development of pelvic, pedal bone, mandibular, and multiple rib fractures. A final—and often disastrous—musculoskeletal complication that may develop in horses with PPID is breakdown of the suspensory apparatus. This condition has been observed more commonly in the hind limbs and often necessitates euthanasia because of the poor response of this painful condition to analgesics.

CLINICOPATHOLOGIC FINDINGS

Abnormal laboratory data in horses with PPID may include mild anemia, an absolute or relative neutrophilia, and an absolute or relative lymphopenia. Although one or more of these abnormalities is usually found in a third or more of equids afflicted with PPID, the true prevalence is not well documented. As well as being increased in number, neutrophils in affected animals may appear hypersegmented. This finding reflects maturity of neutrophils and can be attributed to a longer half-life of circulating neutrophils because cortisol excess limits diapedesis from the vasculature. Eosinopenia is also recognized in human and canine patients with hyperadrenocorticism but is difficult to document in horses because equidae typically have low numbers of circulating eosinophils.

The most common abnormality detected on serum biochemical evaluation is mild to moderate hyperglycemia, which is reported in 25% to 75% of cases, depending on the upper end of the reference range used. Additional abnormal biochemical findings may include elevated liver enzyme activity, hypercholesterolemia, and hypertriglyceridemia. These changes may reflect fat infiltration of the

liver in more advanced cases or possibly a degree of steroid hepatopathy.

DIAGNOSIS

Practically, the diagnosis of PPID is most commonly made by observation of hirsutism and other clinical signs in older equids. Although diagnosis by clinical examination is likely to be accurate in more advanced cases, establishing a diagnosis of PPID in less severely affected horses can be challenging. As a result, a number of endocrinologic tests have been used, but not all of these diagnostic tests have been validated in horses in which the diagnosis was confirmed by subsequent necropsy examination. Further, only limited data compare results of various endocrine tests in horses with presumptive or necropsy confirmed PPID.

Plasma Cortisol Concentration and Loss of Diurnal Cortisol Rhythm

Although hyperadrenocorticism can be accompanied by an elevated plasma cortisol concentration, resting cortisol concentration does not routinely exceed the upper end of the reference range in horses with PPID. Thus measurement of plasma cortisol concentration alone is not a valid diagnostic test. Because plasma cortisol concentration has been well documented to have a diurnal rhythm of secretion and an increase in the morning hours, loss of the diurnal rhythm has been advanced as an accurate screening tool for evaluation of horses with suspected PPID. However, substantial interindividual variation and the effects of external stressors and disease on plasma cortisol make loss of cortisol rhythmicity a poor screening tool for PPID.

Dexamethasone Suppression Test

The dexamethasone suppression test (DST) is considered the "gold standard" endocrine test for support of a diagnosis of PPID by many equine clinicians. However, this statement is not without controversy, and variation among testing protocols can potentially lead to different results. Further concern—although poorly documented—that administration of dexamethasone may exacerbate laminitis in affected equids exists. In its most simple form, the overnight DST consists of measuring cortisol in the late afternoon (typically 5 PM), following this with administration of dexamethasone (40 µg/kg, IM) and subsequently measuring plasma cortisol concentration 17 to 19 hours later (between 10 AM and noon the following day).

Although at present the overnight DST is considered the most accurate endocrine test for supporting a diagnosis of PPID, it does not have 100% sensitivity or specificity. Thus results must always be interpreted in combination with clinical signs. Furthermore, the difference between test results that reveal partial suppression versus complete suppression (to a value <1 µg/dl \approx 30 pmol/L) remains unclear. It would seem logical that horses with partial suppression would have less severe disease than horses with essentially no suppression, but such an assumption cannot currently be supported by either clinical or *post mortem* data. Further, because the natural progression of

PPID remains unknown (and likely varies between affected equidae), whether *pars intermedia* pathology may be present for months or years before DST results become abnormal is unclear. Nevertheless, for veterinarians working in an ambulatory practice, the overnight DST is currently the most practical and best-validated supportive endocrine test for confirmatory diagnosis of PPID in suspect horses.

Thyrotropin Stimulation Test and Combined Dexamethasone Suppression/Thyrotropin Stimulation Test

Thyrotropin (TRH) is a releasing hormone for several pituitary hormones that has been shown to increase plasma cortisol concentration when administered to horses and ponies with Cushing's disease. In contrast, no increase in plasma cortisol concentration was observed in normal horses after TRH administration. Although the TRH stimulation test has not been as well validated as the DST, it often has been used in horses with laminitis because of concerns about exacerbating foot pain following dexamethasone administration. When used, a 30% increase in cortisol concentration between 15 and 90 minutes after administration of TRH supports a diagnosis of PPID. However, interpretation of the response is complicated by variability of the initial cortisol concentration.

To obviate the problem of variability of initial cortisol concentration with the TRH stimulation test, a combined DST/TRH stimulation test has been developed; 3 hours before TRH administration, dexamethasone (40 µg/kg) is administered to suppress cortisol concentration to similar values in both PPID-affected and normal horses. Cortisol concentration is subsequently measured before and 30 minutes after TRH administration. Equids with PPID show an increase in comparison to a lack of change in normal animals. After 24 hours, plasma cortisol concentration remains suppressed in normal horses while it returns to the basal (predexamethasone) concentration in PPID-affected horses. Although this combined test appears to improve the accuracy of the TRH stimulation test, it has not been demonstrated to be any more sensitive or specific for diagnosis of PPID. Further, it is both more expensive for the client and less practical for the ambulatory clinician than the overnight DST. As a consequence, this combined test has not been widely used.

Plasma Adrenocorticotropin Concentration

Horses with PPID typically have excessive amounts of ACTH in abnormal *pars intermedia* tissue and increased amounts of ACTH are released into plasma. Thus plasma ACTH concentration would seem a likely choice for a single sample test to support a diagnosis of PPID. In fact, increased plasma ACTH concentrations—with a maximum reported value of 12,000 pg/ml—have been documented in several reports of PPID in equids. In general, an ACTH concentration that exceeds 27 and 50 pg/ml (\sim 6 and \sim 11 pmol/L) in ponies and horses, respectively, has a high sensitivity for diagnosis of PPID.

Limitations of using plasma ACTH concentration as the only endocrine test to support a diagnosis of PPID are that

sample handling can be problematic and that different laboratories may use different assays for measuring ACTH. Because ACTH can be adsorbed onto glass and can be degraded by proteolytic enzymes in both whole blood and plasma, collection into plastic tubes prefilled with enzyme inhibitors, rapid separation from red cells, and freezing of plasma before shipment for analysis has been recommended. Practitioners who are interested in using ACTH concentration as a diagnostic aid should contact the testing laboratory before sample collection for sample handling recommendations and should only send samples to a laboratory that uses an assay that has been validated as specific for ACTH in equine plasma.

Serum Insulin Concentration

Many equids with PPID—especially ponies—have insulin insensitivity, and the frequency of hyperinsulinemia appears to be greater than that of hyperglycemia. As a consequence, an elevated fasting serum insulin concentration could support a diagnosis of PPID. However, hyperinsulinemia can accompany other metabolic disorders, including a recently described peripheral Cushing's syndrome (see Chapter 16.3: "Peripheral Cushingoid Syndrome ['Equine Metabolic Syndrome'] Induced Cardiac or Skeletal Muscle Necrosis"). Thus use of serum insulin concentration alone as a supportive test for diagnosis of PPID can be misleading because hyperinsulinemia is not specific to PPID.

Urinary Corticoid-to-Creatinine Ratio

Because collection of urine from equids is not as convenient as in other domestic species, measurement of urinary corticoids has not been studied in detail as a supportive test for horses with suspected PPID. In a recent report of seven equids with clinical and histologically confirmed PPID, a urinary corticoid:creatinine ratio greater than 20×10^{-6} had a sensitivity of 100% (range of $25\text{--}110 \times 10^{-6}$ in PPID affected animals in comparison to a range of $4.7\text{--}16 \times 10^{-6}$ in normal horses). Thus this diagnostic test may have use in the evaluation of horses with PPID, but further validation is needed.

TREATMENT

Treatment of equids with PPID initially involves attention to general health care along with a variety of management changes to improve the condition of older animals. In the earlier stages of PPID, when hirsutism and hyperhidrosis may be the primary complaints, body clipping to remove the long hair coat may be the only treatment required. Because many affected animals are aged, routine dental care and correction of dental abnormalities cannot be overemphasized. In addition, reassessment of the diet and incorporation of pelleted feeds designed specifically for older equids should be pursued. Sweet feed and other concentrates high in soluble carbohydrate are best avoided (unless that is all that they will eat), especially when patients are hyperinsulinemic. Also, affected equids may have to be separated from herd mates if they are not getting adequate access to feed. Unfortunately, because the abdomen may become somewhat pendulous, the severity of weight

loss and muscle wasting in more severely affected animals may not be well recognized by owners. In these instances, measurement of body weight and estimation with a weight tape are important parameters to monitor during treatment. Because the major musculoskeletal complication of PPID is recurrent or chronic laminitis, regular hoof care is essential to lessen the risk of flare-ups. Because many PPID-affected patients may also have secondary infections, long-term administration of antibiotics—typically a potentiated sulfonamide—may often be necessary.

Medications that have been used to treat equids with PPID include serotonin antagonists (cyproheptadine), dopamine agonists (pergolide mesylate), and—less commonly—inhibitors of adrenal steroidogenesis (o,p'-DDD and trilostane). Cyproheptadine was one of the initial drugs used because serotonin had been shown to be a potent secretagogue of ACTH in isolated rat *pars intermedia* tissue. Early indications that cyproheptadine ($0.6\text{--}1.2$ mg/kg^{3/4} PO q24h [65–125 mg to a 500-kg horse]) results in clinical improvement and normalization of laboratory data within 1 to 2 months have been disputed because a similar response has been obtained with improved nutrition and management. The margin of safety of cyproheptadine appears to be high; several horses have received twice the recommended dose twice daily without untoward effects. Mild ataxia has been observed in some horses treated with cyproheptadine.

Because loss of dopaminergic innervation appears to be an important pathophysiologic mechanism for PPID, treatment with dopaminergic agonists represents a logical approach to therapy. Pergolide administered in both "high-dose" ($0.006\text{--}0.01$ mg/kg, PO q24h [3–5 mg to a 500-kg horse]) and "low-dose" (0.002 mg/kg, PO q24h [1 mg/day for a 500-kg horse]) protocols has been reported as an effective treatment. Adverse effects of pergolide include anorexia, diarrhea, and colic; however, the latter problems are more often associated with higher doses of the drug. Usually, only transient anorexia is recognized during the initial week of "low-dose" pergolide treatment and can be overcome by cutting the dose in half for 3 to 5 days. Because pergolide is an ergot alkaloid and may also have vasoconstrictive effects, concerns about exacerbation of laminitis have been raised with use of this drug. At present, this concern appears to be largely theoretical; no documented cases in which induction or worsening of laminitis could be attributed to treatment with pergolide have been reported.

Until recently, the main limitation of pergolide treatment for many equids with PPID was expense. However, the following three developments have made pergolide therapy worthy of reconsideration: (1) cyproheptadine has become more costly; (2) "low-dose" (0.002 mg/kg PO q24h [1 mg/day for a 500-kg horse]) pergolide treatment has been documented to be successful in affected horses; and (3) several compounding pharmacies now offer pergolide at a lesser cost. A pertinent yet unanswered question is whether pergolide and cyproheptadine have synergistic effects in the treatment of PPID. Anecdotal reports suggest that greater improvement may be observed when the medications are used concurrently. Finally, it is important to remember that, at present, treatment with either pergolide or cyproheptadine remains both empiric

and off-label; pharmacologic studies of the drugs have not been performed in equidae. Furthermore, although pregnant mares have been treated with the drugs, safety of use during pregnancy has not been studied in equidae.

At present, this author believes that the initial medical treatment for animals with PPID should be pergolide mesylate at a dose of 0.002 mg/kg, PO q24h. If no improvement is noted within 4 to 8 weeks, the daily dose can be increased by 0.002 mg/kg monthly up to a total dose of 0.01 mg/kg. Alternately, if no or only a limited response is observed with 0.004 to 0.006 mg/kg of pergolide and if endocrine test results remain abnormal, 0.3 to 0.5 mg/kg of cyproheptadine can be added to pergolide therapy. However, it is important to remember that the rate of clinical improvement is higher than that for normalization of hyperglycemia and endocrine test results. Thus measuring blood glucose concentration and performing follow-up endocrine testing (DST or plasma ACTH concentration) regularly (about a month after a change in medication or dose or twice yearly in horses that appear to be stable) are prudent in the management of an equid with PPID.

In addition to medications directed at altering ACTH release by the diseased pituitary gland, drugs that target adrenal steroidogenesis have also been used to treat equids with PPID. Early attempts with the adrenocorticolytic agent *o,p'*-DDD were anecdotally reported to be ineffective. Recently, trilostane (0.4-1.0 mg/kg q24h in feed), a competitive inhibitor of 3- β -hydroxysteroid dehydrogenase, was demonstrated to effectively reverse both clinical signs and abnormal endocrine test results in a series of equine PPID cases. These results suggest that multilevel drug intervention with agents directed against both the pituitary and adrenal glands may have a role in select cases of PPID.

As with many chronic diseases in the horse, specific nutrient supplementation and complementary or alternative therapies—including acupuncture, homeopathy, and herbal remedies—have been recommended and used in horses with PPID. Both magnesium and chromium supplementation have been advocated for supportive treatment of this condition. Magnesium supplementation (to achieve a dietary calcium:magnesium ratio of 2:1) has been recommended because magnesium deficiency appears to be a risk factor for insulin insensitivity and type 2 diabetes in humans and because anecdotal reports suggest that supplementation may help horses with obesity-associated laminitis. Similarly, chromium supplementation is recommended to improve carbohydrate metabolism (specifically glucose uptake) and to improve insulin sensitivity in type 2 diabetes. Supplementation with chromium tripicolinate has been demonstrated to increase glucose uptake during a glucose tolerance test in normal yearlings.

An herbal product made from chasteberry recently has been advocated on the Internet for treatment of PPID. However, the claim was supported with a series of case testimonials in which the diagnosis of PPID was poorly doc-

umented. It warrants mention that the two apparently more advanced cases of PPID showed minimal improvement while on the herbal remedy (one horse developed pneumonia, at which time pergolide treatment was reinstated). To date, no controlled studies have been performed to support these nutritional or nontraditional recommendations for management of animals with PPID.

PROGNOSIS

PPID is a lifelong condition. Thus the prognosis for correction of the disorder is poor. However, PPID can be effectively treated with a combination of management changes and medications, which renders the prognosis for life guarded to fair. Little longitudinal study of horses with PPID has been undertaken, but in one report survival time from initial diagnosis to development of complications that necessitated euthanasia ranged from 120 to 368 days in four untreated horses. Furthermore, numerous anecdotal reports discuss horses being maintained for several years as long as response to medical treatment was good and close patient monitoring and follow-up was performed.

Supplemental Readings

- Beech J: Treatment of hypophyseal adenomas. *Comp Cont Educ Pract Vet* 1994; 16:921-923.
- Boujon CE, Bestetti GE, Meier HP et al: Equine pituitary adenoma: a functional and morphological study. *J Comp Pathol* 1993; 109:163-178.
- Couëtil L, Paradis MR, Knoll J: Plasma adrenocorticotropin concentration in healthy horses and in horses with clinical signs of hyperadrenocorticism. *J Vet Intern Med* 1996; 10:1-6.
- Dybdal NO: Pituitary pars intermedia dysfunction (equine Cushing's-like disease). In Robinson NE (ed): *Current Therapy in Equine Medicine*, 4th edition, pp 499-501, Philadelphia, WB Saunders, 1997.
- Dybdal NO, Hargreaves KM, Madigan JE et al: Diagnostic testing for pituitary pars intermedia dysfunction in horses. *J Am Vet Med Assoc* 1994; 204:627-632.
- Heinrichs M, Baumgärtner W, Capen CC: Immunocytochemical demonstration of proopiomelanocortin-derived peptides in pituitary adenomas of the pars intermedia in horses. *Vet Pathol* 1990; 27:419-425.
- Hillyer MH, Taylor FRG, Mair TS et al: Diagnosis of hyperadrenocorticism in the horse. *Equine Vet Educ* 1992; 4:131-134.
- Love S: Equine Cushing's disease. *Br Vet J* 1993; 149:139-153.
- Schott HC, Coursen CL, Eberhart SW et al: The Michigan Cushing's project. In *Proceedings of the 47th Annual Convention of the American Association of Equine Practitioners*, pp 22-24, 2001.
- van der Kolk JH: Diseases of the pituitary gland, including hyperadrenocorticism. In Watson TD (ed): *Metabolic and Endocrine Problems of the Horse*, pp 41-49, London, WB Saunders, 1998.
- van der Kolk JH: Equine Cushing's disease. *Equine Vet Educ* 1997; 9:209-214.

CHAPTER 16.3

Peripheral Cushingoid Syndrome
(‘Equine Metabolic Syndrome’)

PHILIP J. JOHNSON
Columbia, Missouri

Obesity is a very common medical problem in modern horses, largely as a result of the impositions and requirements of modern management practices. In many respects, the tendency for adult horses to develop obesity and the endocrinopathic consequences of obesity-associated insulin insensitivity closely parallels human adult-onset diabetes mellitus. Non-insulin-dependent diabetes (type 2 diabetes mellitus) is currently recognized internationally as an emerging disease of widespread significance. The rapid spread of type 2 diabetes in humans has been directly attributed to a modern life-style of insufficient exercise and dietary excess. Modern horse management practices call for both the imposition of protracted periods of inactivity (stall confinement) and the provision of overly starchy rations.

The modern horse is an excellent example of successful evolution. However, evolution equipped the equine metabolism for survival based on the seasonally variable availability of forage (grass). The temporary development of additional body fat (relative obesity) at times when forage is plentiful provides a survival adaptation for times when conditions are harsh and forage is scarce. During periods in which forage is relatively unavailable, the body fat stores are depleted to provide energy for survival. Under many modern horse management systems, the combination of feeding starch-rich rations for many years and protracted periods of stall confinement can cause domesticated horses to gain and maintain substantial body fat.

The development of obesity in adult horses is attended by a risk for laminitis. In this regard, obesity in mature horses is strikingly similar to the risk for type 2 diabetes mellitus and cardiovascular diseases in obese human patients. As was once the case for obese people, obese horses are commonly diagnosed with hypothyroidism and treated with thyroid hormone supplementation. However, obesity and laminitis are not characteristics of bona fide hypothyroidism in horses. Although an association exists between the development of laminitis and *pars intermedia* dysfunction in old horses, the tendency of younger adult horses (8-18 years) to develop laminitis with obesity should not be attributed to dysfunction in either the thyroid or pituitary glands.

The term *peripheral cushingoid syndrome* has been widely adopted by veterinary practitioners in recent years to identify these mature, adult horses that develop laminitis in the face of obesity. The word *cushingoid* implies that the clinical features of this syndrome should be attributed to

excess glucocorticoid (GC) actions. As this article will discuss, abnormal regulation of GC at the cellular level in some tissues may play an important role in some aspects of this condition, but the endocrinopathic characteristics of this condition are certainly not restricted to those associated with GC excess. Although more than 10 different syndrome labels have variously referred to the analogous human condition during the past several years, it was recently decided that this condition in humans would be referred to as the *metabolic syndrome*. Accordingly, it has been advocated that the equine peripheral cushingoid syndrome should probably be more appropriately termed the *equine metabolic syndrome*.

OBESITY AND THE INSULIN REFRACTORY STATE

The development of obesity in both human and equine individuals directly causes insulin insensitivity, also known as the *insulin refractory state*. Recent discoveries have forced veterinary practitioners to reevaluate their thinking about adipocytes. Fat tissue is not, as was previously thought, simply a benign and metabolically inactive energy storage tissue. Multiple metabolically active factors are secreted by adipocytes that exert actions locally through paracrine and autocrine mechanisms and systemically through endocrine mechanisms. These factors inhibit the action of insulin at central (hepatic) and peripheral (skeletal muscle and adipocytes) tissues. Inhibited insulin responsiveness leads to the development of glucose intolerance.

Glucose intolerance is defined as an abnormally delayed reduction in the rate by which exogenous glucose, such as that derived from food in the intestinal tract, is removed from the circulation. Consequences of glucose intolerance include persistent postprandial hyperglycemia, prolonged release of insulin by pancreatic β -cells, and fasting hyperglycemia. Disposition of a glucose load by insulin should normally entail the inhibition of hepatic gluconeogenesis and stimulation of glucose uptake by the peripheral tissues, especially skeletal muscle and adipose tissue. Unlike human and feline patients in whom chronic insulin insensitivity and glucose intolerance commonly lead to pancreatic β -cell failure (endocrine pancreatic exhaustion) and a progressive reduction in insulin secretion (non-insulin-dependent diabetes mellitus), affected horses are different in that they

appear to be able to maintain a high level of insulin secretion in the face of insulin resistance. The development of marked hyperglycemia is uncommon in these horses.

An insulin refractory state can be demonstrated in horses affected with the peripheral cushingoid syndrome in which the fasting serum insulin concentration is often extremely high (hyperinsulinemia). In many affected horses, the serum insulin concentration exceeds 1000 pmol/L (reference range, <300 pmol/L). However, overt type 2 diabetes, as indicated by hyperglycemia and reduced serum insulin concentration, appears not to occur in horses very often.

A discussion of the mechanics of the development of insulin insensitivity as a consequence of obesity is beyond the scope of this article. Specific endocrine signals produced by adipocytes that are thought to cause insulin insensitivity in the obese state include resistin, leptin, free fatty acids, interleukin-6, and cortisol. Adipocytes possess the steroid transformation enzyme 11 β -hydroxysteroid dehydrogenase-1 (11 β -HSD-1) that converts circulating cortisone to active cortisol. In the human metabolic syndrome and in certain types of equine laminitis, tissue activity of 11 β -HSD-1 is increased such that the local production of cortisol is increased. Cortisol is derived by conversion from the circulating inactive metabolite, cortisone. Local tissue dysregulation of cortisol as a result of increased 11 β -HSD-1 expression is the basis for the use of the term *peripheral cushingoid syndrome*. A satisfactory explanation for the association between increased 11 β -HSD-1, increased cortisol, and the development of laminitis in this syndrome is currently lacking. The interested reader is directed to other sources for further information regarding the pathophysiology of obesity-related insulin insensitivity (see Supplemental Readings).

It should be noted that excessive levels of endogenous and exogenous GC are an important cause of insulin insensitivity. Insulin insensitivity is therefore evident in equine conditions associated with excess GC, including *pars intermedia* dysfunction, stress (especially stress associated with painful laminitis), and the administration of exogenous GC such as dexamethasone and triamcinolone.

Albeit controversial, a direct laminitis-inducing action for GC has been suggested by the development of laminitis in horses affected with *pars intermedia* dysfunction and in some horses that are treated with dexamethasone and triamcinolone. Several researchers have reported that laminitis cannot be predictably and directly induced by GC. However, the novel concept that laminitis is caused by cardiovascular dysfunction resulting from insulin insensitivity and glucose intolerance in these horses has received much attention recently.

INSULIN INSENSITIVITY LEADING TO ENDOTHELIAL CELL DYSFUNCTION

In the insulin refractory state, hyperglycemia arises because the action of insulin is inhibited in hepatocytes, adipocytes, and skeletal muscle cells. Other tissues not dependent on insulin for glucose uptake are consequently subjected to relatively high levels of glucose during periods of insulin insensitivity. Of these tissues, endothelial cells are particularly susceptible to the untoward effects of

relative glucose excess, collectively known as *glucotoxicity*. Substantial evidence exists to implicate a central and critical role for endothelial dysfunction in the pathogenesis of vascular complications attributable to insulin insensitivity in humans. Moreover, only moderate levels of hyperglycemia are needed to cause endothelial dysfunction.

Several mechanisms by which excessive glucose leads to endothelial dysfunction have been demonstrated. Increased glucose availability leads to the generation of oxygen-derived free radicals (oxidative stress), an overall reduction in endothelial-derived nitric oxide (NO) activity, and increased expression of endothelin-1 (ET-1). The combination of reduced NO and enhanced ET-1 production leads to a relatively increased state of vasospasticity because NO and ET-1 are the two most potent endothelium-derived vasorelaxing and vasoconstricting factors, respectively. In addition to the effect on endothelial regulation of underlying vascular tone, hyperglycemic states also tend to cause endothelial cells, which normally present a relatively anti-thrombotic surface to blood, to be transformed into a relatively procoagulative state. Another important component of the procoagulative state that tends to develop as a result of insulin insensitivity is enhanced platelet aggregability. The reader is directed to other sources for more information on this subject (see Supplemental Readings).

INSULIN INSENSITIVITY DURING STRESSFUL CONDITIONS

Any condition associated with stress should be regarded as a potential trigger for increased endogenous cortisol production and GC-induced insulin refractoriness. An excellent clinical example of this situation is laminitis itself. The development of painful laminitis for any reason leads to a pronounced stress response. Affected horses develop hypercortisolemia, hyperinsulinemia, hyperglycemia, glucose intolerance, and hypertension. Therefore the veterinary practitioner must be careful to differentiate between stress-induced insulin refractoriness that arises because of laminitic pain versus insulin insensitivity that is the underlying cause of laminitis. Accordingly, a diagnosis of obesity-associated insulin refractoriness might not be possible to establish during bouts of painful laminitis because the pain itself will lead to hyperinsulinemia.

OBESITY AND LAMINITIS

Experimental investigations on the development of laminitis in mature horses with obesity have not been reported. Almost all research aimed at a better understanding of the pathogenesis of equine laminitis has addressed alimentary-type acute laminitis. The author contends that laminitis that arises in conjunction with peripheral cushingoid syndrome in mature horses is probably not attributable to intestinally derived factors or circulatory changes associated with endotoxemia. Instead, obesity-associated laminitis is a manifestation of insulin insensitivity and glucose intolerance in obese horses. Nevertheless in both scenarios the pathologic changes at the level of the hoof that lead to clinical laminitis may be similar in that both alimentary- and endocrinopathic-type laminitis

appear to involve perturbations in the regulation of blood flow through the lamellae and local oxidative stress.

Although laminitis in conjunction with the peripheral cushingoid syndrome certainly may be very painful and destructive to the hoof-lamellar interface, it is more typically reported to be insidious and mild. Owners commonly report that affected horses have never exhibited lameness. Horse owners commonly fail to recognize the development of the characteristic divergent growth lines at the hoof wall of affected horses. In many cases, the diagnosis of laminitis in obese horses is an incidental finding during a routine physical examination. Therefore it appears that in many instances laminitis that occurs in conjunction with obesity may be subclinical and might not cause pain and recognizable lameness. Instead the pathologic processes within the hoof-lamellar interface progressively lead to lengthening of the lamellae, widening of the white-line zone, and divergent growth lines ("laminar lines" or "stress lines") in the hoof wall.

It has been suggested that obesity predisposes to laminitis because the increased weight leads to excessive tension in the deep digital flexor tendon (DDFT) and that heavier horses are more likely to develop laminitis because of relatively greater distractive forces at the hoof-lamellar interface. Although weight-associated tension in the DDFT surely plays a role in the morbidity of laminitis after the acute phase for any cause, the fact that pony breeds are at greater risk for the development of laminitis than horse breeds suggest that the obesity factor is not a simple matter of greater or lesser force in the DDFT. Interestingly, compared with horses, pony breeds tend to be refractory to insulin and glucose intolerant.

CLINICAL SIGNS AND DIAGNOSIS

Horses affected with metabolic syndrome are usually obese and tend to be aged between 8 and 18 years. However, it should be noted that not all affected horses are grossly obese and that horse owners often dislike use of the term *obesity*. Although this syndrome may be recognized in all breeds, some breeds appear to be genetically predisposed to developing obesity and the health risks that attend it. Of note, the author has observed that the domesticated Spanish Mustang, Paso Fino, Peruvian Paso, and the Morgan horse appear to be at particular risk for this condition. Compared with horses, several pony breeds tend to be relatively insulin insensitive and prone to glucose intolerance. This difference might help to explain why ponies are at greater risk for laminitis.

The exterior appearance of affected horses commonly includes development of increased subcutaneous fat in the neck ("cresty neck") and the rump, but most affected horses tend to be distinctly obese in a generalized manner. A body score of 7 to 9 (of 9) is often assigned to affected horses. Geldings tend to develop a "swollen sheath" because of enhanced subcutaneous adiposity. Ample adipose tissue is also identified in the omental location for most of these horses at necropsy. Horse owners invariably report that it is very difficult to reduce the weight of these horses by dietary restriction and they are commonly referred to as *easy-keepers*. Affected broodmares sometimes exhibit abnormal estrous cycling and may be difficult to breed successfully.

Horses affected with the peripheral cushingoid syndrome are sometimes presented to veterinarians for the treatment of laminitis. In other cases the presence of an obese phenotype and the development of hoof wall changes consistent with chronic subclinical laminitis are recognized incidentally during a routine examination. Inspection of feet from affected horses commonly reveals evidence of chronic laminitis including a convex sole, divergent growth lines, and widening of the white line zone. Radiographic findings may include evidence of pedal bone displacement (rotation) and pedal bone remodeling ("pedal osteitis").

The presence of other endocrinopathic conditions such as hypothyroidism and *pars intermedia* dysfunction should be ruled out with appropriate diagnostic tests. Hypothyroidism should be ruled out on the basis of the results of a thyroid stimulation test, and *pars intermedia* dysfunction should be ruled out on the basis of the results of a dexamethasone suppression test. Both serum triiodothyronine (T3) and thyroxine (T4) levels tend to be low in horses affected with the peripheral cushingoid syndrome.

Hyperinsulinemia in the presence of a normal or slightly elevated glucose concentration in the fasted animal supports diagnosis of peripheral cushingoid syndrome in obese horses. Although the resting plasma glucose concentration tends to be normal or slightly elevated, affected horses may develop very marked elevations in serum insulin concentration. Serum-free fatty acid levels are often elevated.

Glucose intolerance may be specifically corroborated and characterized on the basis of the results of an intravenous glucose tolerance test (IVGTT). After the horse has been fasted for 12 hours, a resting (zero-time) blood glucose determination is made and the horse is then injected with glucose (0.5 g/kg of body weight IV given during approximately 3 to 4 minutes) with a 50% dextrose solution. Blood glucose concentration is determined at every 30 minutes for 3 hours while the horse is fasted. A state of glucose intolerance is suggested by a failure of the blood glucose to return to the baseline within 3 hours. Other factors that might cause false-positive identification of the insulin refractory state and hyperinsulinemia include pain from laminitis, stress/excitement, exogenously administered GC, and *pars intermedia* dysfunction.

At present, diagnosis of the peripheral cushingoid syndrome (obesity-associated insulin refractory state) is based on consideration of the physical appearance of the patient, results of routine blood tests, fasting hyperinsulinemia, elimination of other reasonable causes of similar findings and the results of glucose tolerance testing.

TREATMENT AND PREVENTION

As with human beings, the crucial and most effective preventive and treatment strategies are increased physical activity and dietary-induced weight reduction. Increased exercise has been shown to improve insulin sensitivity in horses and ponies. For horses affected with painful laminitis, increased activity might be detrimental until laminitis has been controlled. Effective management of laminitis will also enable the horse to exercise and lead to reduction in the secretion of endogenous GC. The common

practice of feeding growing and mature horses and ponies rations characterized by a high glycemic index (excessive grain) should be discouraged. Careful attention to ration formulation should include consideration of the size of the horse and the level of physical activity. Many horses develop obesity because they are fed too much grain in respect to their level of exercise; obese horses are commonly stall-confined for protracted periods and exercised at mild-to-moderate levels of energy expenditure for short periods.

Ideally, consultation with an equine nutritionist should be recommended. A carefully-planned low-starch ration (low glycemic index) that contains high-quality forage that is balanced with respect to minerals and vitamins is recommended for the management of horses affected with the peripheral cushingoid syndrome. The widespread practice of feeding inappropriately high quantities of grain to younger horses should be discouraged because these horses tend to progress to obesity in middle age and become prone to laminitis. Dietary supplementation with fat should not be recommended because lipids contribute to the development of endothelial dysfunction in other species ("lipotoxicity"). The extent to which lipids contribute to the pathogenesis of cardiovascular dysfunction in affected horses, whose diet normally contains very low levels of lipid, is currently unknown.

Although dietary thyroid hormone supplementation is commonly advocated in the management of obesity and obesity-associated laminitis, this practice has been discredited in the human field. Inappropriate thyroid supplementation may certainly lead to weight reduction in these patients by creating a state of iatrogenic hyperthyroidism. Potentially adverse side effects of inappropriate thyroid supplementation, which have been well documented in human patients, have received little attention in equine patients. Similarly, no basis exists for the treatment of insulin refractoriness in equine patients with either pergolide or cyproheptadine, both of which should be reserved for the management of hyperadrenocorticism associated with bona fide *pars intermedia* dysfunction.

In light of the evidence that oxidative stress is important for the pathogenesis of endothelial dysfunction in the obese state and that antioxidant strategies have been shown to improve endothelial function in affected individuals, dietary supplementation with high levels of vitamin E (10,000 units PO q12h) might be safely used in the management of obese horses in conjunction with weight reduction, dietary changes, and increased activity.

Enhanced platelet aggregability in the obese patient might be addressed with orally administered aspirin therapy. Pharmacologic reversal of the vasoconstrictive actions of ET-1 may be useful for the management of laminitis associated with obesity, however, these agents have not yet been investigated in horses. Similarly, based on work in other species, inhibitors of the renin-angiotensin system may reverse some of the pathologic vascular changes associated with endothelial dysfunction in obese horses, but these drugs have also not been investigated in horses. Recently introduced antidiabetic (insulin-sensitizing) drugs that increase the action of insulin in peripheral tissues, such as the thiazolidinedione, metformin, are deserving of investigation in equine patients. Thiazolidinedione antidiabetic agents are also potent inhibitors of 11 β -HSD-1

and appear to preferentially and selectively reduce visceral fat accumulations in humans. However, to this author's knowledge none of the many drugs aimed at human patients have been investigated in horses at this time. Reviews of the role of antiglycemic, antidiabetic agents in the management of type 2 diabetes in human patients are available.

Some speculation exists that inhibitors of enzymes involved in the biosynthetic pathway for cortisol (including metyrapone, aminoglutethimide, ketoconazole, miconazole, and trilostane) might be useful for the management of both *pars intermedia* dysfunction and metabolic syndrome. However, at this time few data have been published to support efficacy and safety for administration of these pharmaceuticals in equine patients. Trilostane is a 3 β -hydroxysteroid dehydrogenase inhibitor that acts to inhibit adrenal steroidogenesis. In one study, trilostane (0.5-1.0 mg/kg PO q24h) caused improvement in both the clinical signs (laminitis, polydipsia/polyuria, lethargy) and results of endocrinologic tests in horses affected with *pars intermedia* dysfunction. Furthermore, treatment with trilostane reduced the quantity of phenylbutazone that was needed for the management of pain in those horses that were affected with severe laminitis. During a concurrent investigation, trilostane also caused clinical improvement in horses affected with the peripheral cushingoid syndrome (Cathy McGowan, personal communication, London, England, 2002). In other studies, the effectiveness and safety of trilostane has been questioned.

Although insulin insensitivity has also been attributed to specific deficiencies of chromium, inorganic phosphate, magnesium, and vanadium, the extent to which deficiencies in these micronutrients is likely to contribute to the morbidity of obesity in equine patients is likely insignificant. Chromium supplementation has been reported to improve insulin sensitivity in other species, but in one equine study orally administered chromium L-methionine (0.02 mg/kg) failed to improve insulin sensitivity in old mares. Further investigation into the therapeutic value of either chromium, magnesium, or vanadium supplementation for insulin insensitive horses is warranted.

Supplemental Readings

- Boden G: Pathogenesis of type 2 diabetes: insulin resistance. *Endocrinol Metab Clin North Am* 2001; 30:801-815.
- Bujalaska IJ, Kumar S, Stewart PM: Does central obesity reflect "Cushing's disease of the omentum?" *Lancet* 1997; 349:1210-1213.
- Cosentino F, Luscher TF: Endothelial dysfunction in diabetes mellitus. *J Cardiovasc Pharmacol* 1998; 32(Suppl 3):S54-S61.
- Freestone JF, Beadle R, Shoemaker K et al: Improved insulin sensitivity in hyperinsulinaemic ponies through physical conditioning and controlled feed intake. *Equine Vet J* 1992; 24:187-190.
- Garcia MC, Beech J: Equine intravenous glucose tolerance test: glucose and insulin responses of healthy horses fed grain or hay and of horses with pituitary adenoma. *Am J Vet Res* 1986; 47:570-572.
- Giugliano D, Ceriello A, Paolisso G: Oxidative stress and diabetic vascular complications. *Diabetes Care* 1996; 19:257-267.
- Masuzaki H, Paterson J, Shinyama H et al: A transgenic model of visceral obesity and the metabolic syndrome. *Science* 2001; 294:2166-2170.

- Montague CT, O'Rahilly S: The perils of portliness: causes and consequences of visceral adiposity. *Diabetes* 2000; 49:883-888.
- Poitout V, Robertson RP: Minireview: secondary β -cell failure in type 2 diabetes—a convergence of glucotoxicity and lipotoxicity. *Endocrinology* 2002; 143:339-342.
- Rask E, Olsson T, Soderberg S et al: Tissue specific dysregulation of cortisol metabolism in human obesity. *J Clin Endocrinol Metabol* 2001; 86:1418-1421.
- Schiekofer S, Balletshofer B, Andrassy M et al: Endothelial dysfunction in diabetes mellitus. *Semin Thromb Hemost* 2000; 26:503-511.
- Shuldiner AR, Yang R, Gong D-W: Resistin, obesity, and insulin resistance—the emerging role of the adipocyte as an endocrine organ. *N Engl J Med* 2001; 345:1345-1346.
- Steppan CM, Bailey ST, Bhat S et al: The hormone resistin links obesity to diabetes. *Nature* 2001; 409:307-312.
- Taylor AA: Pathophysiology of hypertension and endothelial dysfunction in patients with diabetes mellitus. *Endocrinol Metab Clin North Am* 2001; 30:983-997.
- Ting HH, Timimi FK, Boles KS et al: Vitamin C improves endothelium-dependent vasodilatation in patients with non-insulin-dependent diabetes mellitus. *J Clin Invest* 1996; 97: 22-28.
- Uemura S, Matsushita H, Li W et al: Diabetes mellitus enhances vascular matrix metalloproteinase activity: role of oxidative stress. *Circ Res* 2001; 88:1291-1298.
- Watts GE, Playford DA: Dyslipoproteinemia and hyperoxidative stress in the pathogenesis of endothelial dysfunction in non-insulin dependent diabetes mellitus: an hypothesis. *Atherosclerosis* 1998; 41:17-30.

CHAPTER 16.4

Anhidrosis

JEREMY D. HUBERT

RALPH E. BEADLE

Baton Rouge, Louisiana

GARY NORWOOD

Metairie, Louisiana

Equine anhidrosis has been recognized as a clinical condition of horses since the early 1920s. This condition is characterized by the inability of the horse to sweat effectively in response to appropriate stimuli and by the resulting clinical signs. The disease is predominant in hot, humid climates such as the American Gulf Coast states and is not necessarily associated with acclimatization stress. Horses native to regions where the disease is prevalent are just as likely to be affected as are imported horses. Any horse can be affected, and no predilection is apparent for the disease with respect to coat color, age, sex, or breed, although an increased frequency of anhidrosis may occur in horses in training and a decreased frequency in adolescent horses. The precise pathophysiology of anhidrosis has not been elucidated but altered sweat gland function with potential down-regulation or desensitization of the sweat gland β_2 -receptors may be involved.

CLINICAL SIGNS

Although poor performance may be the initial complaint, tachypnea is probably the first indication that an affected horse may be suffering from anhidrosis. Although inappropriate tachypnea is evident at the outset of anhidrosis, affected horses are typically not presented to veterinarians until the owner recognizes signs of overt exercise intolerance. The extent to which the respiratory rate is elevated varies according to the severity of the disease. Horses with

severe anhidrosis may even be tachypneic at rest. Horses with partial anhidrosis may breathe rapidly for extended periods of time after exercise, with respiratory rates of as high as 120 breaths per minute. The latter animals still retain an ability to sweat, however, the response is diminished and not appropriate for the stimulus.

A useful guideline regarding the likelihood that a horse may be affected with anhidrosis is the time taken for the rectal temperature to return into the reference range after exercise. In severe cases the body temperature may not return to normal levels. A normal horse should cool out within 30 minutes. If the rectal temperature remains elevated for longer than 30 minutes, it should be suspected that the horse may be suffering from anhidrosis. Clinical recognition of tachypnea in affected horses often leads veterinarians to include respiratory diseases, obstructive or restrictive, in the differential diagnosis of anhidrosis. When the disease becomes more severe, other signs may be noted. A decreased sweat response indicates anhidrosis, and in some horses the ability to sweat may be lost completely. In horses affected with partial anhidrosis, sweating may be preserved in some areas of the horse's integument. Under the mane, in the inguinal, axillary, and perineal regions, and in those areas under the saddle or halter, the ability to sweat may be retained somewhat. Chronic cases of anhidrosis reveal a dry, flaky skin with areas of alopecia, especially about the face and along the neck. The latter horses are often anorexic, lethargic, and

- Montague CT, O'Rahilly S: The perils of portliness: causes and consequences of visceral adiposity. *Diabetes* 2000; 49:883-888.
- Poitout V, Robertson RP: Minireview: secondary β -cell failure in type 2 diabetes—a convergence of glucotoxicity and lipotoxicity. *Endocrinology* 2002; 143:339-342.
- Rask E, Olsson T, Soderberg S et al: Tissue specific dysregulation of cortisol metabolism in human obesity. *J Clin Endocrinol Metabol* 2001; 86:1418-1421.
- Schiekofer S, Balletshofer B, Andrassy M et al: Endothelial dysfunction in diabetes mellitus. *Semin Thromb Hemost* 2000; 26:503-511.
- Shuldiner AR, Yang R, Gong D-W: Resistin, obesity, and insulin resistance—the emerging role of the adipocyte as an endocrine organ. *N Engl J Med* 2001; 345:1345-1346.
- Steppan CM, Bailey ST, Bhat S et al: The hormone resistin links obesity to diabetes. *Nature* 2001; 409:307-312.
- Taylor AA: Pathophysiology of hypertension and endothelial dysfunction in patients with diabetes mellitus. *Endocrinol Metab Clin North Am* 2001; 30:983-997.
- Ting HH, Timimi FK, Boles KS et al: Vitamin C improves endothelium-dependent vasodilatation in patients with non-insulin-dependent diabetes mellitus. *J Clin Invest* 1996; 97: 22-28.
- Uemura S, Matsushita H, Li W et al: Diabetes mellitus enhances vascular matrix metalloproteinase activity: role of oxidative stress. *Circ Res* 2001; 88:1291-1298.
- Watts GF, Playford DA: Dyslipoproteinemia and hyperoxidative stress in the pathogenesis of endothelial dysfunction in non-insulin dependent diabetes mellitus: an hypothesis. *Atherosclerosis* 1998; 41:17-30.

CHAPTER 16.4

Anhidrosis

JEREMY D. HUBERT

RALPH E. BEADLE

Baton Rouge, Louisiana

GARY NORWOOD

Metairie, Louisiana

Equine anhidrosis has been recognized as a clinical condition of horses since the early 1920s. This condition is characterized by the inability of the horse to sweat effectively in response to appropriate stimuli and by the resulting clinical signs. The disease is predominant in hot, humid climates such as the American Gulf Coast states and is not necessarily associated with acclimatization stress. Horses native to regions where the disease is prevalent are just as likely to be affected as are imported horses. Any horse can be affected, and no predilection is apparent for the disease with respect to coat color, age, sex, or breed, although an increased frequency of anhidrosis may occur in horses in training and a decreased frequency in adolescent horses. The precise pathophysiology of anhidrosis has not been elucidated but altered sweat gland function with potential down-regulation or desensitization of the sweat gland β_2 -receptors may be involved.

CLINICAL SIGNS

Although poor performance may be the initial complaint, tachypnea is probably the first indication that an affected horse may be suffering from anhidrosis. Although inappropriate tachypnea is evident at the outset of anhidrosis, affected horses are typically not presented to veterinarians until the owner recognizes signs of overt exercise intolerance. The extent to which the respiratory rate is elevated varies according to the severity of the disease. Horses with

severe anhidrosis may even be tachypneic at rest. Horses with partial anhidrosis may breathe rapidly for extended periods of time after exercise, with respiratory rates of as high as 120 breaths per minute. The latter animals still retain an ability to sweat, however, the response is diminished and not appropriate for the stimulus.

A useful guideline regarding the likelihood that a horse may be affected with anhidrosis is the time taken for the rectal temperature to return into the reference range after exercise. In severe cases the body temperature may not return to normal levels. A normal horse should cool out within 30 minutes. If the rectal temperature remains elevated for longer than 30 minutes, it should be suspected that the horse may be suffering from anhidrosis. Clinical recognition of tachypnea in affected horses often leads veterinarians to include respiratory diseases, obstructive or restrictive, in the differential diagnosis of anhidrosis. When the disease becomes more severe, other signs may be noted. A decreased sweat response indicates anhidrosis, and in some horses the ability to sweat may be lost completely. In horses affected with partial anhidrosis, sweating may be preserved in some areas of the horse's integument. Under the mane, in the inguinal, axillary, and perineal regions, and in those areas under the saddle or halter, the ability to sweat may be retained somewhat. Chronic cases of anhidrosis reveal a dry, flaky skin with areas of alopecia, especially about the face and along the neck. The latter horses are often anorexic, lethargic, and

do not appear to drink adequate amounts of water. These signs may be similar to horses with decreased thyroid function, however, thyroidectomized horses appear to sweat normally.

DIAGNOSIS

A presumptive diagnosis of anhidrosis may be made on the basis of clinical signs, occurrence of the condition in hot, humid conditions, and by ruling out respiratory disease. Results of hematology and a serum biochemical profile are not specific for anhidrosis. Dehydration may be evidenced by prerenal azotemia and possibly a high urine specific gravity. Definitive diagnosis is based on intradermal testing to evaluate the sweating response of the horse's integument. With the use of specific β_2 -agonists, a semiquantitative test for anhidrosis has been used in Thoroughbred horses. At sites on the neck below the mane, salbutamol sulfate or terbutaline sulfate are injected intradermally in dilutions from 10^{-3} w/v to 10^{-8} w/v and compared with a negative control injection of physiologic saline. The results are evaluated 20 to 30 minutes later. Sweating will occur at all sites except the control site in normal horses (Figure 16.4-1, A). Horses with severe anhidrosis may not sweat at any of the dilutions, whereas

horses with partial anhidrosis may respond at the 10^{-4} w/v and 10^{-6} w/v sites (Figure 16.4-1, B).

A skin biopsy may be performed. Histopathologic findings have been described as thickened basal lamina, evidence of poor myoepithelial contraction, thickened connective tissues, and marked reduction of vesicles in the secretory cells. The lumen of the duct of the sweat gland is often obstructed with cellular debris.

TREATMENT

At present no predictably effective medical treatments exist for this disease. Management and environmental control are still the most appropriate way to try to resolve anhidrosis. Horses that succumb to acute episodes are prone to other heat stress-related conditions, and prompt action to attempt to reduce the body temperature and treat the hyperthermia must be taken. The horse should be cooled with cold water and immediately placed in a cooler environment.

The physical activities of affected horses should be restricted. During periods of relatively high ambient temperature, accommodation of the horse in a well-shaded stall with constant air movement, such as that provided by a fan, should minimize heat stress. Misting fans will help cool the environment as will running cool water on the roof of the barn. Activity should only occur during the early morning or late evening. After exercising, the horse should be assisted in cooling off by being hosed down with water. The normal diet of the horse should be maintained; however, concentrated rations should be minimized whenever possible. Oral electrolyte supplements are often recommended. Potassium salts (60 g of KCl or Lite Salt) can be added to the water or feed. When electrolytes are added to the water, an additional source of drinking water must be supplied that does not contain electrolyte to ensure adequate water intake. Administration of an electrolyte replacement product (Entrolyte He, Pfizer, Exton, Pa.) has been recommended in acute cases of anhidrosis. In older anecdotal reports, the use of iodinated casein (10-15 g/day for 4-8 days) and vitamin E (1000-3000 U PO q24h) for a month have been reported as helping the condition. Successful management of affected horses following treatment with levothyroxine has also been reported. Although there may be similarities with hypothyroidism, care should be taken with use of thyroid supplements as the resultant increase in metabolic rate could potentially cause an anhidrotic horse to overheat if exercised in very hot, humid weather.

Anecdotal reports have advocated use of a commercially available product containing L-tyrosine, ascorbic acid, niacin, and cobalt (One AC, MP, Phoenix, Ariz.). The success of this treatment is reported to be variable. Tyrosine might theoretically be involved in the resensitization of sequestered β_2 -receptors and acts as a precursor for the formation of dopamine and thus catecholamines. However, plasma tyrosine concentrations are not decreased in horses with anhidrosis. A reduction in workload simultaneous with this treatment for 3 weeks is beneficial. Some practitioners administer this supplement to horses with a history of anhidrosis at the outset of the "anhidrosis season."

Anecdotal reports also exist to suggest that clenbuterol may be helpful in the management of anhidrosis. Mild

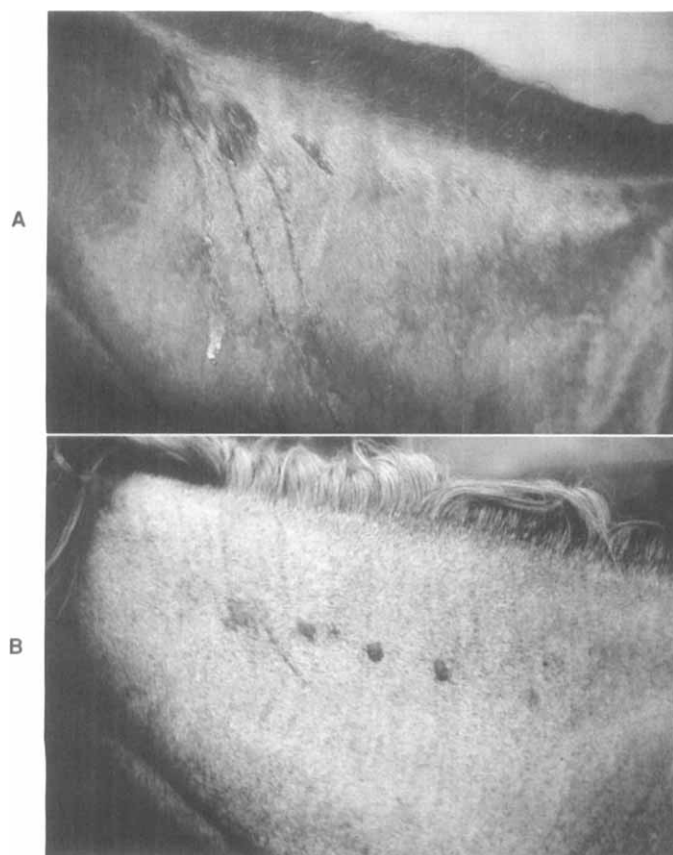


Figure 16.4-1 Response to intradermal injection of a β_2 -adrenergic agonist such as terbutaline sulfate in a normal horse (A) and a horse with partial anhidrosis (B). Dose-dependent sweating is visible over the injection sites in the normal horse. Sweating is much less in the horse with anhidrosis.

sweating is a well-recognized side effect of clenbuterol when it is used to treat respiratory conditions in horses. However, in light of the fact that exogenously-administered β_2 -agonists have been shown to promote prolonged desensitization of the sweat gland, this therapy is not currently recommended.

The use of drugs to decrease sympathetic drive would seem to be logical in treating horses with anhidrosis. Methyldopa has been used by some practitioners with reported success. An initial dosage of 3000 mg every 24 hours was used and was increased to 4000 mg every 24 hours if no positive response occurred in 3 to 4 days. When a horse with anhidrosis is treated with this drug, the concentration of epinephrine at the β_2 -adrenergic receptor site may decrease, which may allow receptor reexpression. Despite anecdotal reports of success, no controlled studies exist regarding the efficacy of this agent in horses with anhidrosis.

Patients should be observed closely when being treated; normal thermoregulatory responses should allow a return to normal body temperature within 30 minutes after exer-

cise. Counting the respiratory rate when the horse is at rest and after it has exercised may help the veterinarian to identify resolution of the problem. With severe, chronic cases, relocation of the horse to a more temperate climate to relieve the heat stress may be the only option. After relocation, affected horses will require as long as 6 weeks to begin to sweat normally. It should be emphasized to horse owners that anhidrosis will likely recur when the hot, humid season arrives and that this problem may become lifelong.

Supplemental Readings

- Evans CL: Physiological mechanisms that underlie sweating in the horse. *Br Vet J* 1966; 122:117-123.
- Hubert JD, Beadle RE: Equine anhidrosis. *Comp Cont Educ* 1998; 20; 846-851.
- Mayhew IG, Ferguson HO: Clinical, clinicopathologic, and epidemiologic features of anhidrosis in central Florida Thoroughbred horses. *J Vet Intern Med* 1987; 1:136-141.

SECTION XVII

Urinary System

Edited by Dr. Harold C. Schott II

CHAPTER 17.1

Examination of the Urinary System

ELIZABETH A. CARR
East Lansing, Michigan

HISTORY AND PHYSICAL EXAMINATION

To evaluate a horse with urinary tract disease, the clinician should collect a complete history and perform a thorough physical examination. Important historic information includes diet, medications administered, response to treatment, number of horses affected, and duration and type of clinical signs. Water intake and urinary output should also be assessed. For example, owners may mistake pollakiuria, frequent urination, for polyuria, increased urine production. Differentiation between these two conditions is helpful to form a diagnostic plan. Pollakiuria is frequently seen in females during estrus or with cystic calculi or cystitis in both sexes. In contrast, polyuria more commonly accompanies renal disease, diabetes insipidus, diabetes mellitus, pituitary pars intermedia dysfunction, and behavioral problems such as psychogenic water drinking or salt eating. Astute owners may note increased thirst following exercise or a change in urine appearance, such as a clearer stream, to support the presence of polydipsia and polyuria.

Clinicians can determine water intake during a 24-hour period by turning off automatic watering devices and providing a known volume of water to the horse. Water intake may vary widely with diet, environmental conditions, and level of activity so that repeated measurements during several 24-hour periods may be more rewarding in documenting average daily water consumption. Horses stabled in a cool climate and fed a large amount of the diet as a concentrate may drink as little as 15 to 20 L daily, whereas horses exercising in hot climates have been recorded to drink as much as 90 L daily. Urine output, which should range between 5 and 15 L in a horse with normal renal function, is more difficult to determine. Urine collection harnesses can be applied for 24-hour urine collections; alternately, indwelling Foley catheters

attached to a collection apparatus can be used to quantify urine output. Although these methods are fairly well tolerated by horses used for research, they have limited application to the clinical patient.

The most common presenting complaints for horses with urinary tract disease are weight loss and abnormal urination. Other clinical signs vary with the etiology and location of the problem and may include colic, fever, anorexia, depression, ventral edema, oral ulceration, excessive dental tartar, or scalding of the perineum or hind legs. Although lumbar pain and hindlimb lameness have been attributed to urinary tract disease, a musculoskeletal problem is the usual cause of these clinical signs. A decrease in performance may be an early presenting complaint for renal disease, but poor performance is more likely a result of the mild anemia and lethargy that accompany uremia rather than a consequence of renal pain.

In addition to a thorough physical examination, rectal palpation should be included in the evaluation of all horses with suspected urinary tract disease. The bladder should be palpated to determine size, wall thickness, and presence of cystic calculi or mural masses. If the bladder is full, palpation should be performed again after bladder catheterization or voiding. The caudal pole of the left kidney can be palpated for size and texture. The ureters are generally not palpable unless enlarged or obstructed by disease, but the retroperitoneal course of the ureters in the dorsal abdomen to the trigone should be palpated to determine if ureters can be detected. In mares, palpation of the distal ureters through the vaginal wall may be more rewarding. Dilation of a ureter may occur with pyelonephritis or ureteral calculi. The reproductive tract should also be palpated to assess whether a reproductive problem could be a possible cause of the clinical signs.

HEMATOLOGY AND SERUM BIOCHEMISTRY

Results of a complete blood count revealing an elevated white blood cell count and elevated total protein or fibrinogen concentration support an inflammatory or infectious disease process. Mild anemia, indicated by a packed cell volume of 20% to 30%, consequent to decreased erythropoietin production and a shortened red blood cell lifespan, may be found in horses with chronic renal failure.

Blood urea nitrogen (BUN) and serum creatinine concentrations are the most commonly used indices of renal function, specifically glomerular filtration rate (GFR). It is important to remember that increases in BUN and creatinine do not occur until the majority of nephrons, usually approximately 75%, become nonfunctional. For example, complete loss of function of one kidney does not result in increases in BUN or creatinine as long as contralateral renal function remains normal. Thus these parameters are not very useful in evaluating early or minor changes in GFR. Once elevated, however, small increases in BUN and creatinine are more sensitive indicators of further deterioration in GFR because a doubling of BUN or creatinine can be interpreted as a 50% decline in remaining renal function.

Azotemia may also be prerenal or postrenal in origin. Prerenal azotemia is a result of decreased renal perfusion, whereas postrenal azotemia is a result of obstruction of the urinary tract. Thus interpretation of serum chemistry test results should be made in light of hydration status of the patient and other presenting signs. Although specific threshold values for BUN and creatinine that differentiate renal disease from prerenal azotemia do not exist, measures of urine concentration (see following section on urinalysis) or the urine-to-serum creatinine ratio can provide useful information. Urine-to-serum creatinine ratios in excess of 50:1 (reflecting concentrated urine) are expected in horses with prerenal azotemia, whereas ratios less than 37:1 were reported in a group of horses diagnosed with primary renal disease. Creatinine is a charged molecule that is less membrane permeable than urea; therefore, acute changes in renal function are more accurately reflected by changes in creatinine than in BUN, and the increase in creatinine is proportionately greater than the rise in BUN. This fact has led to use of the BUN-to-creatinine ratio to differentiate prerenal azotemia or acute renal failure from chronic renal failure. With acute renal compromise, a BUN-to-creatinine ratio of less than 10:1 is expected, whereas the ratio should exceed 15:1 in cases of chronic renal failure. Although the BUN-to-creatinine ratio may be useful to consider, the values are not always reliable, especially with chronic renal failure in which BUN may vary considerably according to dietary protein intake.

In addition to BUN and creatinine, serum electrolyte, protein (albumin and globulin) and glucose concentrations, and muscle enzyme activities should be included in the laboratory database. Hypochloremia is the most consistent electrolyte abnormality seen in horses with polyuric renal failure. Hyponatremia has been variably reported in horses with renal disease and is most commonly found with urinary tract disruption and uroperitoneum. Serum potassium concentration is usually normal but may be elevated in cases of acute renal failure or uroperitoneum. Calcium and phosphorus concentrations vary in

horses with renal disease. Hypercalcemia and hypophosphatemia are often found in horses with chronic renal failure, especially when fed alfalfa hay, whereas hypocalcemia and hyperphosphatemia are more common with acute renal failure. With protein-losing glomerulopathies, albumin tends to be lost to a greater extent than globulin because of the former's lower molecular weight. Although low total protein and albumin concentrations can accompany chronic renal disease in many species, horses appear more refractory to development of hypoproteinemias and the nephrotic syndrome. In fact, some patients have an increase in globulin concentration that suggests chronic antigenic stimulation associated with neoplasia, glomerulonephritis, pyelonephritis, or amyloidosis. Hyperglycemia (blood glucose >175-200 mg/dl) that results from stress, exercise, sepsis, pituitary pars intermedia dysfunction, or diabetes mellitus may result in glucosuria. In cases for which pigmenturia is a complaint, muscle enzyme activities are helpful to differentiate myoglobinuria from hematuria or hemoglobinuria.

URINALYSIS

Urinalysis should be performed in all horses in which urinary tract disease is suspected. Urine can be collected midstream while the horse is voiding, by urethral catheterization, or by cystocentesis in foals. Color, clarity, odor, viscosity, and specific gravity should be evaluated at the time of collection. Normal equine urine is pale yellow to deep tan in color and is often turbid because of large amounts of calcium carbonate crystals and mucus. Urine appearance often changes during urination, especially toward the end of micturition when more crystals tend to be voided. If pigmenturia or hematuria is present, the clinician should note the timing and duration of discolored urine passage to help in localizing the source. Pigmenturia throughout urination is most consistent with myonecrosis or a bladder or kidney lesion, whereas passage of discolored urine at the start or end of urination is more commonly seen with lesions of the urethra or accessory sex glands.

Urine specific gravity is a measure of the amount of solute in urine, and is a useful estimate of urine concentration. In response to water deprivation, a horse with normal renal function should be able to produce concentrated urine with a specific gravity between 1.025 and 1.050. In contrast, foals typically have urine that is more dilute than serum (i.e., hyposthenuria or a specific gravity <1.008) consequent to a high-volume milk diet. Although the constant polyuria decreases their ability to generate a large osmotic gradient in the medullary interstitium, foals can produce urine with a specific gravity higher than 1.030 when dehydrated. With renal disease, the ability to produce either concentrated (specific gravity >1.025) or dilute (specific gravity <1.008) urine is lost. Thus horses with chronic renal failure typically manifest isosthenuria, in which urine is produced that has an osmolality similar to that of serum (specific gravity of 1.008-1.014).

In horses that present with dehydration or shock resulting from a number of problems, measurement of urine-specific gravity can help to differentiate prerenal from re-

nal azotemia. A high urine-specific gravity (>1.035) supports prerenal azotemia, whereas failure to concentrate urine in the face of dehydration supports a diagnosis of renal disease. It should be emphasized that specific gravity measurement is most valid in the first urine sample voided after fluid therapy is initiated, because successful fluid therapy leads to production of dilute urine. Other disorders that may result in a decreased ability to concentrate urine in the face of dehydration include septicemia or endotoxemia, nephrogenic diabetes insipidus, washout of the medullary interstitium, or pituitary or hypothalamic diseases that lead to central diabetes insipidus.

The pH of equine urine is usually alkaline (7.5-9.0). High-intensity exercise or bacteriuria can result in acidic pH. The latter can further result in an ammonia odor to the sample because of breakdown of urea by bacteria with urease activity. Production of more dilute urine usually results in a decrease in urine pH toward the neutral value. Commercially available urine reagent strips can yield false-positive results for protein when alkaline samples are tested. Thus the clinician can better assess proteinuria by performing the semiquantitative sulfosalicylic acid precipitation test or by specific quantification with a colorimetric assay (as for cerebrospinal fluid) and by comparing the result with urine creatinine concentration in the form of a urine protein-to-creatinine ratio. Although not well documented in horses, a value above 1.0, which is the threshold value for proteinuria used in small animal patients, appears appropriate for use in horses at this time.

Proteinuria may occur with pyuria, bacteriuria, glomerular disease, or transiently following exercise. Normal equine urine should not contain glucose. Glucosuria may accompany hyperglycemia associated with the causes described earlier or with administration of dextrose-containing fluids or parenteral nutrition products. In addition, glucosuria may accompany sedation with α_2 -agonists or exogenous corticosteroid administration. When glucosuria is detected in the absence of hyperglycemia, primary tubular dysfunction should be suspected. A positive result for blood on a urine reagent strip can result from the presence of hemoglobin, myoglobin, or intact red blood cells in the urine sample. Evaluation of serum for hemolysis and of urine sediment for red blood cells (RBCs), combined with an ammonium sulfate precipitation test to detect myoglobin, can help to differentiate between these pigments.

Urine sediment should be evaluated for cells, casts, and bacteria within 30 to 60 minutes after collection. Fewer than 5 RBCs per high-power field (hpf) can be seen in an atraumatically collected urine sample. Increases in the number of urinary RBCs/hpf can result from inflammation, infection, toxemia, neoplasia, or exercise. Pyuria (>5 white blood cells/hpf) is seen most commonly with infectious or inflammatory disorders. Casts are molds of protein and cells that form in tubular lumens and subsequently pass into the bladder. They are rare in normal equine urine but may be found with inflammatory or infectious processes. Casts are relatively unstable in alkaline urine; thus evaluation of urine sediment should be performed as soon as possible after collection to ensure accurate assessment. Normal equine urine should have few to no bacteria. The absence of bacteria on sediment evalua-

tion does not rule out their presence, however, and bacterial culture of urine collected by catheterization or cystocentesis, in foals, should be performed in suspected cases of pyelonephritis or cystitis.

Equine urine is rich in crystals. The majority of these are calcium carbonate crystals of variable size, but triple phosphate crystals and an occasional calcium oxalate crystal can also be seen in normal equine urine. In some samples, addition of a few drops of a 10% acetic acid solution may be necessary to dissolve crystals for accurate assessment of urine sediment.

γ -Glutamyl transferase (GGT) is an enzyme located in the brush border of epithelial cells lining renal tubules. The presence of GGT activity in urine arises from proximal renal tubular cell turnover, and the activity increases with renal tubular damage and sloughing of epithelium into the tubular lumen. Values for urine GGT activity are expressed as a ratio to urine creatinine concentration, as follows, with a value higher than 25 considered abnormal:

$$\frac{\text{Urinary GGT activity}}{(\text{uCr} \times 0.01)}$$

Use of this ratio in equine urine appears to be a sensitive indicator of tubular damage and has been advocated for use as an early indicator of tubular damage as well as a monitoring aid in horses on nephrotoxic drug therapy. Unfortunately, elevated urine GGT-to-creatinine ratios can be found with dehydration and after the initial dose or two of nephrotoxic medications. Thus although results may reflect renal tubular damage, in practical situations the ratio has been deemed too sensitive and currently is not used as much as when the test was originally described.

FRACTIONAL CLEARANCE OF ELECTROLYTES

Fractional clearance of electrolytes is used to evaluate the secretory or reabsorptive function of renal tubules. Fractional clearances are expressed as a percentage of endogenous creatinine clearance as in the following equation:

$$\text{Fractional clearance A} = \frac{[\text{Urine A}] \times [\text{Plasma creatinine}]}{[\text{Plasma A}] \times [\text{Urine creatinine}]} \times 100$$

The equine kidneys function to reabsorb more than 99% of filtered sodium, whereas little potassium is conserved. Thus normal fractional clearance values are less than 1% for sodium and 15% to 65% for potassium (Table 17.1-1). Increases in fractional clearance values, specifically for sodium and phosphorus, are early indicators of renal tubular damage. However, fractional sodium clearance can be artifactually increased in horses receiving intravenous polyionic solutions.

WATER DEPRIVATION

Water deprivation is a simple test used to determine whether hyposthenuric polyuria is caused by a behavioral problem such as psychogenic polydipsia or is the result of

Table 17.1-1
Fractional Clearance of Electrolytes in Horses

Electrolyte	Normal Ranges
Na ⁺	0.02-1.00
Cl ⁻	0.04-1.60
K ⁺	15-65*
PO ₄ ⁻	0.00-0.50†
Ca ⁺⁺	0.00-6.72‡

*Fractional clearance of K⁺ may exceed upper limit on high K⁺ diets.

†Fractional clearance of PO₄⁻ exceeding 4% suggests excessive intake.

‡Fractional clearance of Ca⁺⁺ should exceed 2.5% with adequate intake.

central or nephrogenic diabetes insipidus. A water deprivation test should not be performed in an animal that is clinically dehydrated or azotemic. A baseline urinalysis from a sample collected by catheterization to empty the bladder at the start of the test and measurement of serum BUN and creatinine concentrations and body weight should be performed before removal of food and water. Urine-specific gravity and weight loss are measured after 12 hours (usually overnight) and 24 hours. The test should be stopped when urine-specific gravity reaches 1.025 or greater, a loss of 5% of body weight occurs, or dehydration becomes apparent.

With long-standing psychogenic polydipsia, affected horses may not have fully concentrated urine because of washout of the medullary interstitial osmotic gradient. In such patients little benefit is gained from extension of the test period beyond 24 hours. However, affected horses should respond to water deprivation more favorably by producing urine with a higher specific gravity after a period of partial water deprivation during which daily water intake is restricted to 40 ml/kg for several days. This restriction period should allow time for restoration of the medullary interstitial osmotic gradient. Horses with central or nephrogenic diabetes insipidus cannot concentrate urine in response to a water-deprivation test. When these problems are suspected, patients should be monitored every 4 to 6 hours because significant dehydration may ensue within 6 hours of water deprivation.

EXOGENOUS VASOPRESSIN ADMINISTRATION

Horses that fail to concentrate urine in response to water deprivation are considered to have diabetes insipidus (DI). DI is an endocrine cause of polyuria that is termed central or neurogenic when caused by a lack of vasopressin (antidiuretic hormone) production and secretion or nephrogenic when caused by a lack of response of collecting ducts to vasopressin (see Chapter 17.4: "Differential Diagnosis of Polyuria/Polydipsia"). Exogenous vasopressin administration is a diagnostic test that can be used to differentiate neurogenic from nephrogenic DI. In the past, vasopressin extracted from pituitary glands and stored in oil was used for diagnostic purposes, but this product is no longer available. In humans and small animals with polyuria, desmopressin acetate (DDAVP), a synthetic vasopressin analog, is now used for diagnosis and treatment of neurogenic DI. Recently it has been demonstrated that intravenous (IV) administration of 20 µg of DDAVP (equal in antidiuretic activity to 80 IU of vasopressin) is both a safe and useful diagnostic tool for evaluation of horses with DI. The preparation comes as a nasal spray for humans (100 µg DDAVP/ml) and IV administration of 0.2 ml (at a cost of approximately \$10) produced an increase in urine-specific gravity to values greater than 1.020 in normal horses in which polyuria and hyposthenuria (specific gravity <1.005) was induced by repeated nasogastric intubation with water.

entiate neurogenic from nephrogenic DI. In the past, vasopressin extracted from pituitary glands and stored in oil was used for diagnostic purposes, but this product is no longer available. In humans and small animals with polyuria, desmopressin acetate (DDAVP), a synthetic vasopressin analog, is now used for diagnosis and treatment of neurogenic DI. Recently it has been demonstrated that intravenous (IV) administration of 20 µg of DDAVP (equal in antidiuretic activity to 80 IU of vasopressin) is both a safe and useful diagnostic tool for evaluation of horses with DI. The preparation comes as a nasal spray for humans (100 µg DDAVP/ml) and IV administration of 0.2 ml (at a cost of approximately \$10) produced an increase in urine-specific gravity to values greater than 1.020 in normal horses in which polyuria and hyposthenuria (specific gravity <1.005) was induced by repeated nasogastric intubation with water.

ENDOSCOPY

Endoscopy of the urinary tract is a useful diagnostic aid in patients presenting with abnormal urination. In addition, it can be used to determine whether a patient has two functional kidneys when one kidney cannot be imaged during ultrasonographic examination. A flexible endoscope with an outside diameter of 12 mm or less and a minimal length of 1 m is adequate for examination of the urethra and bladder of an adult horse of either sex. Sterilization of the endoscope should be performed before endoscopy of the lower urinary tract. Tranquilization of the patient is recommended, and the distal end of the penis or the vulva should be thoroughly cleansed. The endoscope is passed in a manner identical to that for a catheter, with the air control intermittently used to inflate the urethra or bladder. Normal urethral mucosa is pale pink with longitudinal folds. When dilated with air the mucosa flattens and may appear more red than normal, and a prominent vascular pattern may be apparent.

Passage of a catheter before endoscopy for sample collection or to empty the bladder can result in mild irritation and erythema of the urethral mucosa. These signs should not be interpreted as abnormal findings. The regions of the ischial arch where the urethra begins to widen into the ampullar portion and of the colliculus seminalis in the roof of the pelvic urethra just distal to the urethral sphincter should be closely examined, because these are common sites of posturination or postbreeding hemorrhage in the gelding or stallion.

Subsequent passage of the endoscope through the urethral sphincter coupled with air distention allows evaluation of the bladder for presence of calculi, inflammation, or masses. Observation of the ureteral openings in the dorsal aspect of the trigone can help determine the source of hematuria or pyuria. A small volume of urine should pass from each ureteral opening asynchronously, approximately once each minute. The clinician can perform ureteral catheterization to obtain urine samples from each kidney by passing a sterile polyethylene catheter through the biopsy channel of the endoscope. In addition, biopsy of masses in the bladder or urethra can be performed.

ULTRASONOGRAPHY, RADIOGRAPHY, AND NUCLEAR SCINTIGRAPHY

Ultrasonographic examination of the urinary tract can be performed transrectally or transabdominally. Imaging of the bladder is best performed transrectally by using a 5-MHz probe. While imaging the bladder, the clinician should remember that equine urine is an inhomogeneous, echogenic fluid because of the presence of mucus and crystals. Presence of a cystic calculus can be confirmed, because calculi have a highly echogenic surface and produce an acoustic shadow. Similarly, masses in the bladder wall may be both imaged and palpated during the examination.

The right kidney is triangular or horseshoe-shaped and is best imaged transabdominally through the dorsolateral extent of the last two to three intercostal spaces. The left kidney is bean-shaped and lies deep to the spleen in the left paralumbar fossa. Because the left kidney is deeper than the right kidney, it can be difficult to image completely and is best examined with a 2.5- or 3-MHz probe. The size and shape of both kidneys and the structure and echogenicity of the parenchyma should be assessed. In acute renal failure the kidneys are normal to increased in size; however, the corticomedullary junction may be indistinct. Chronic renal failure may result in kidneys that are smaller and more echogenic than normal. Cystic or mineralized areas within renal parenchyma may be associated with chronic renal disease or congenital anomalies. Calculi within the renal pelvis generally cast an acoustic shadow and can result in hydronephrosis of the affected kidney. Occasionally, one or both kidneys cannot be imaged because of the presence of gas-filled bowel between the kidney and abdominal wall. Reexamination at a later time is usually required for successful imaging in such cases.

Radiography is rarely used in evaluation of urinary tract disease in the horse. Diagnostic radiographs of the urinary tract usually can only be obtained in foals or Miniature Horses. Excretory urography is useful if the clinician suspects a nonfunctional kidney or seeks to identify hypoplastic kidneys or ectopic ureters. The procedure is infrequently used and requires general anesthesia. Retrograde contrast studies can be used in foals suspected of having a ruptured bladder. The technique may also assist in identifying strictures or masses in the urethra or bladder; however, endoscopy is a more useful tool to diagnose these problems.

Nuclear scintigraphic imaging can be used to assess renal anatomy and to provide a qualitative assessment of renal function. Indications for renal scintigraphy are to document the presence of a functional kidney when multiple ultrasonographic examinations have been complicated by interfering bowel or when unilateral nephrectomy is being considered. The former question may be more easily answered by observation of urine flow from the ureteral openings during cystoscopy. Renal scintigraphic studies have used technetium 99m (^{99m}Tc) tagged to the radiopharmaceutical's glucoheptonate (GH), which is taken up by the proximal tubular epithelial cells to provide anatomic detail, diethylenetriaminopentaacetic acid (DTPA), which is similar to inulin in that it is neither secreted nor reabsorbed after filtration, or mercaptoacetyl-triglycine (MAG_3), which is similar to paraaminohippur-

atein in that it is largely secreted by the tubule and can be used to assess renal blood flow. The radiopharmaceutical ^{99m}Tc -DTPA may also be used to measure GFR without use of an external γ -camera. The procedure requires IV injection of the radiopharmaceutical followed by collection of multiple blood samples during a period of time to produce an elimination curve.

RENAL BIOPSY

Renal biopsy can be useful to determine the region of the nephron affected, the type of lesion, and the chronicity and severity of disease. Although a relatively safe procedure when performed with ultrasonographic guidance, it has inherent risks, including subcapsular hemorrhage and hematuria and, less commonly, penetration of bowel. With the horse sedated and restrained in a stock, penetration of the needle (Tru-cut biopsy needle, Baxter Healthcare, Deerfield, Ill.) into the renal parenchyma can be imaged ultrasonographically by triangulating the ultrasound beam with the biopsy instrument and the kidney. As an alternative, the site and depth of the biopsy can be determined by ultrasonographic imaging immediately before the biopsy. The tissue collected should be placed in formalin for histopathologic evaluation. If desired, additional samples can be collected for bacterial culture and for immunofluorescent testing, which requires tissue storage in Michel's medium.

Although renal biopsy results should, in theory, provide useful information to characterize the renal disease, these results more often document the presence of chronic disease for which the inciting cause cannot be detected except through association with a historic event or immunofluorescent testing. This limitation can be attributed to the fact that 75% or more of nephron function is typically lost before onset of clinical signs. Pathologic lesions are widespread at this point, and involvement of all nephron segments as well as the interstitium may lead to an interpretation of end-stage kidney disease. In the occasional case, the results may aid in separating infectious (pyelonephritis) or congenital (renal dysplasia) from non-specific causes of renal failure. Although such results would assist in the therapeutic approach to these patients, the limitations and risks of renal biopsy should be considered before this diagnostic technique is performed in horses with chronic renal failure.

MEASUREMENT OF GLOMERULAR FILTRATION RATE

GFR is a measure of functional renal mass. Reductions in GFR can occur with primary renal disease, decreased renal perfusion, or obstructive renal disease. Several diagnostic tests are available for estimation of GFR. As already mentioned, serum BUN and creatinine concentrations begin to increase when approximately 75% of functional renal mass becomes compromised. Other more sensitive measures of changes in GFR include endogenous and exogenous creatinine clearances, inulin clearance, sodium sulfanilate clearance, and ^{99m}Tc -DTPA clearance. Performance of these tests requires timed urine collections, repeated blood sampling, and specialized laboratory assays. Thus

these tests have limited clinical use and are primarily used as research tools.

URETHRAL PRESSURE PROFILES

Cystometrography and urethral pressure profiles are used to evaluate detrusor and urethral muscle function. Both techniques involve measurement of intraluminal pressure during inflation of the bladder or urethra through a catheter. These techniques have been useful for diagnosis of myogenic and neurogenic disorders of the bladder and urethra in dogs and humans. The technique has been performed experimentally in normal female horses and ponies, but little information is available about use of these techniques in clinical cases.

Supplemental Readings

- Grossman BS, Brobst DE, Kramer JW et al: Urinary indices for differentiation of prerenal azotemia and renal azotemia in horses. *J Am Vet Med Assoc* 1982; 180:284-288.
- Kohn CW, Chew DJ: Laboratory diagnosis and characterization of renal disease in horses. *Vet Clin North Am Equine Pract* 1987; 3:585-615.
- Matthews HK, Andrews FM, Daniel GB et al: Measuring renal function in horses. *Vet Med* 1993; 88:349.
- Sullins KE, Traub-Dargatz JL: Endoscopic anatomy of the equine urinary tract. *Comp Cont Educ Pract Vet* 1984; 6(11):S663-S668.
- Traub-Dargatz JL, McKinnon AO: Adjunctive methods of examination of the urogenital tract. *Vet Clin North Am Equine Pract* 1988; 4(3):339-358.

CHAPTER 17.2

Urinary Incontinence

BEATRICE T. SPONSELLER
Ames, Iowa

Urinary incontinence is the inability to control urination. It results in the intermittent or continuous escape of urine unrelated to the act of micturition. Causes of incontinence may be nonneurogenic or neurogenic in origin and may include congenital and acquired abnormalities of the lower urinary tract and of its innervation, respectively.

NONNEUROGENIC INCONTINENCE

Nonneurogenic incontinence has been associated with ectopic ureteral insertion and other congenital malformations (see Chapter 17.3: "Congenital Disorders of the Urinary Tract"), urolithiasis (see Chapter 17.5: "Obstructive Disease of the Urinary Tract"), and neoplasia of the lower urinary tract (see Chapter 17.6: "Urinary Tract Neoplasia"). In mares, incontinence may develop after trauma to the external urethral sphincter from breeding accidents or dystocia. Furthermore, iatrogenic trauma resulting from inadvertent insertion of a vaginal speculum into the urethra and bladder has been reported as a cause of incontinence. Although rare, a few cases of estrogen-responsive incontinence resulting from low urethral sphincter tone have been reported in mares. In geldings, a primary myogenic form of bladder paralysis has been described in association with incomplete bladder evacuation, in the absence of neurologic deficits. The resulting accumulation of large amounts of crystalloid sediment in the bladder, termed *sabulous urolithiasis*, causes overstretching and atony of the detrusor muscle. The cause of incomplete bladder evacuation often is elusive, but in some geldings difficulty of attaining normal

urination posture secondary to chronic lumbosacral pain has been suspected. Cystitis is a common feature of most micturition disorders and may cause frequent, involuntary detrusor contractions because of irritation of stretch receptors in the bladder wall, commonly referred to as *urge incontinence*. Primary bacterial cystitis is rare in horses.

NEUROGENIC INCONTINENCE

Neurogenic incontinence implies dysfunction of the neural pathways associated with normal micturition. The latter is a reflex function that involves sacral parasympathetic (pelvic nerve), somatic (pudendal nerve), and lumbar sympathetic (hypogastric nerve) neurons under the central control of the brainstem and cerebral cortex. Neurogenic incontinence can be divided into upper (UMN) and lower (LMN) motor neuron deficits, depending on location of the lesion. Damage to the sacral spinal cord segments or to the pelvic and pudendal nerves results in detrusor and urethral sphincter atony with urinary retention and overflow incontinence (LMN bladder). Causes of lower motor neuron bladder paralysis in the horse include equine herpes virus-1 (EHV-1) encephalomyelopathy (see Chapter 2.2: "Equine Herpesvirus"), cauda equina neuritis (see Chapter 14.6: "Bladder, Rectal, Anal, and Tail Paralysis; Perineal Hypalgesia; and Other Signs of Cauda Equina Syndrome"), sorghum toxicosis, equine protozoal myeloencephalitis (EPM; see Chapter 2.11: "Equine Protozoal Myeloencephalitis"), sacral vertebral trauma, and neoplasia. Additionally, epidural administration of alcohol to show horses may result in iatrogenic bladder paralysis.

these tests have limited clinical use and are primarily used as research tools.

URETHRAL PRESSURE PROFILES

Cystometrography and urethral pressure profiles are used to evaluate detrusor and urethral muscle function. Both techniques involve measurement of intraluminal pressure during inflation of the bladder or urethra through a catheter. These techniques have been useful for diagnosis of myogenic and neurogenic disorders of the bladder and urethra in dogs and humans. The technique has been performed experimentally in normal female horses and ponies, but little information is available about use of these techniques in clinical cases.

Supplemental Readings

- Grossman BS, Brobst DE, Kramer JW et al: Urinary indices for differentiation of prerenal azotemia and renal azotemia in horses. *J Am Vet Med Assoc* 1982; 180:284-288.
- Kohn CW, Chew DJ: Laboratory diagnosis and characterization of renal disease in horses. *Vet Clin North Am Equine Pract* 1987; 3:585-615.
- Matthews HK, Andrews FM, Daniel GB et al: Measuring renal function in horses. *Vet Med* 1993; 88:349.
- Sullins KE, Traub-Dargatz JL: Endoscopic anatomy of the equine urinary tract. *Comp Cont Educ Pract Vet* 1984; 6(11):S663-S668.
- Traub-Dargatz JL, McKinnon AO: Adjunctive methods of examination of the urogenital tract. *Vet Clin North Am Equine Pract* 1988; 4(3):339-358.

CHAPTER 17.2

Urinary Incontinence

BEATRICE T. SPONSELLER
Ames, Iowa

Urinary incontinence is the inability to control urination. It results in the intermittent or continuous escape of urine unrelated to the act of micturition. Causes of incontinence may be nonneurogenic or neurogenic in origin and may include congenital and acquired abnormalities of the lower urinary tract and of its innervation, respectively.

NONNEUROGENIC INCONTINENCE

Nonneurogenic incontinence has been associated with ectopic ureteral insertion and other congenital malformations (see Chapter 17.3: "Congenital Disorders of the Urinary Tract"), urolithiasis (see Chapter 17.5: "Obstructive Disease of the Urinary Tract"), and neoplasia of the lower urinary tract (see Chapter 17.6: "Urinary Tract Neoplasia"). In mares, incontinence may develop after trauma to the external urethral sphincter from breeding accidents or dystocia. Furthermore, iatrogenic trauma resulting from inadvertent insertion of a vaginal speculum into the urethra and bladder has been reported as a cause of incontinence. Although rare, a few cases of estrogen-responsive incontinence resulting from low urethral sphincter tone have been reported in mares. In geldings, a primary myogenic form of bladder paralysis has been described in association with incomplete bladder evacuation, in the absence of neurologic deficits. The resulting accumulation of large amounts of crystalloid sediment in the bladder, termed *sabulous urolithiasis*, causes overstretching and atony of the detrusor muscle. The cause of incomplete bladder evacuation often is elusive, but in some geldings difficulty of attaining normal

urination posture secondary to chronic lumbosacral pain has been suspected. Cystitis is a common feature of most micturition disorders and may cause frequent, involuntary detrusor contractions because of irritation of stretch receptors in the bladder wall, commonly referred to as *urge incontinence*. Primary bacterial cystitis is rare in horses.

NEUROGENIC INCONTINENCE

Neurogenic incontinence implies dysfunction of the neural pathways associated with normal micturition. The latter is a reflex function that involves sacral parasympathetic (pelvic nerve), somatic (pudendal nerve), and lumbar sympathetic (hypogastric nerve) neurons under the central control of the brainstem and cerebral cortex. Neurogenic incontinence can be divided into upper (UMN) and lower (LMN) motor neuron deficits, depending on location of the lesion. Damage to the sacral spinal cord segments or to the pelvic and pudendal nerves results in detrusor and urethral sphincter atony with urinary retention and overflow incontinence (LMN bladder). Causes of lower motor neuron bladder paralysis in the horse include equine herpes virus-1 (EHV-1) encephalomyelopathy (see Chapter 2.2: "Equine Herpesvirus"), cauda equina neuritis (see Chapter 14.6: "Bladder, Rectal, Anal, and Tail Paralysis; Perineal Hypalgesia; and Other Signs of Cauda Equina Syndrome"), sorghum toxicosis, equine protozoal myeloencephalitis (EPM; see Chapter 2.11: "Equine Protozoal Myeloencephalitis"), sacral vertebral trauma, and neoplasia. Additionally, epidural administration of alcohol to show horses may result in iatrogenic bladder paralysis.

In the presence of suprasacral spinal cord or brainstem lesions, urethral sphincter tone is exaggerated and coordination of micturition is lost. The bladder usually is distended firmly and difficult to express (UMN bladder). Bladder function may return through the use of sacral spinal reflexes, but voiding is incomplete, which results in sabulous urolithiasis and eventually loss of detrusor function and overflow incontinence as with lower motor neuron bladder. Incontinence resulting from upper motor neuron dysfunction is rare in horses but may be associated with EHV-1 encephalomyelopathy, EPM, aberrant parasitic migration, or trauma. Occasionally, the underlying cause of neurogenic incontinence remains unidentified.

CLINICAL SIGNS

Horses with urinary incontinence show intermittent or continuous dribbling of urine, which usually is exacerbated by increases in abdominal pressure, such as during exercise, vocalization, or coughing. Other common features include a strong urine odor and scalding of the perineum and proximomedial aspect of the hind limbs of mares and the distodorsal aspect of the hind limbs and ventrum of males. If the incontinence is of neurogenic origin, it may be accompanied by other neurologic deficits. In the case of lower motor neuron dysfunction, urine dribbling is usually continuous, and other signs such as loss of anal and tail tone, fecal retention, hind limb weakness, penile prolapse, and perineal sensory deficits are common. In cases of upper motor neuron dysfunction, urine leakage is initially intermittent, and spinal ataxia may be present. If the urethral sphincter pressure consistently exceeds intravesicular pressure, bladder rupture may occur.

DIAGNOSIS

The diagnosis of urinary incontinence is based on clinical signs, history, and the results of physical and specialty examinations. The latter should include evaluation of the nervous system, rectal palpation, transrectal ultrasonography, and endoscopy of the lower urinary tract. In young foals, excretory urography, pyelography, and cystography may be performed. Evaluation of intravesicular and urethral pressures via cystometrography and urethral pressure profilometry is available at some facilities.

The history may reveal a traumatic incidence such as a dog sitting event or other trauma that involves the sacral spinal area, or it may reveal recent breeding or dystocia in the case of mares. A congenital malformation of the lower urinary tract should be suspected if urinary incontinence has been present since birth, although some forms of congenital malformation, such as frontal septation of the bladder, may not lead to incontinence until later in life. Rectal examination may help distinguish the markedly distended, flaccid, easily expressible "lower motor neuron bladder" from the firmly distended "upper motor neuron bladder" that resists manual pressure. Furthermore, cystic calculi or changes in bladder wall thickness resulting from inflammation or neoplasia can be palpated and imaged by use of ultrasonography. Endoscopic examination of the lower urinary tract allows direct visualization of uroliths, neoplastic disorders, strictures, and other acquired or con-

genital abnormalities. Additional diagnostic procedures such as cerebrospinal fluid analysis and scintigraphic examination of the sacral spine may help differentiate infectious causes from traumatic causes of neurogenic incontinence. Urinary tract infection is a common sequela of micturition disorders and therefore justifies urinalysis and quantitative urine culture in all cases of urinary incontinence. Finally, hematologic parameters may be abnormal if an infectious or inflammatory process is present, and azotemia can occur with significant outflow obstruction or bilateral pyelonephritis.

TREATMENT

Treatment of nonneurogenic incontinence depends on the underlying cause and entails removal of uroliths, surgical correction of ectopic ureters, surgical removal of obstructive scars or masses, and treatment with estradiol benzoate or cypionate (5 to 10 μ g/kg intramuscularly every other day) if estrogen responsive incontinence is suspected. Prognosis for horses with nonneurogenic incontinence is usually good, unless the underlying problem cannot be resolved, as in the case of advanced neoplasia, severe congenital abnormalities, and irreversible myogenic bladder paralysis.

If the incontinence is of neurogenic origin, the bladder should be evacuated three to four times daily by transrectal manual expression or catheterization. This helps avoid development of sabulous urolithiasis and overstretching of the detrusor muscle. Placement of an indwelling catheter through a perineal urethrostomy facilitates repeated bladder evacuation in males. If neurogenic or myogenic bladder paralysis is longstanding and a large amount of crystalloid sediment has accumulated, bladder lavage with large amounts of fluids may be beneficial, if changes in the bladder wall are deemed reversible. Removal of sabulous sludge via cystotomy bears the risk of inadvertent contamination of the peritoneal cavity and is no longer recommended.

When chronic bladder paralysis and complete, irreversible loss of detrusor function occur, the prognosis is poor. If some detrusor activity remains, treatment with bethanechol chloride (0.025-0.075 mg/kg SQ or 0.2-0.4 mg/kg PO q8h), a parasympathomimetic ester that stimulates bladder contraction may be beneficial. Treatment should begin with the smallest dose and be adjusted according to the individual's response. Concurrent administration of a drug that decreases urethral resistance is recommended, especially if upper motor neuron dysfunction is suspected. The α -adrenergic blocker phenoxybenzamine (0.7 mg/kg PO q6h) has been used to decrease proximal urethral tone, but it may be cost prohibitive in the adult horse. Acepromazine (0.02-0.05 mg/kg IM q8h) also has α -adrenergic antagonist activity in addition to its tranquilizing effect. Diazepam (0.02-0.1 mg/kg slowly IV) may be beneficial because it decreases external urethral sphincter tone through its relaxant effect on skeletal muscle.

Antimicrobial therapy should be part of the treatment regimen irrespective of the cause of incontinence. Potentiated sulfonamides (trimethoprim in combination with sulfadiazine or sulfamethoxazole, 25 mg/kg PO q12-24h) have a broad spectrum of antimicrobial activity, are concentrated in the urine, and may be used prophylactically

or therapeutically, if urine culture yields a susceptible pathogen. Additionally, skin areas affected by urine leakage should be cleansed daily, dried thoroughly, and covered with zinc oxide ointment or petrolatum to prevent scalding. Treatment should be continued until the incontinence has resolved. Unfortunately, prognosis for horses with incontinence of neurogenic origin is usually poor, unless caused by a specific, potentially treatable or self-limiting neurologic disease such as EPM or EHV-1 encephalomyelopathy.

Supplemental Readings

Booth TM, Howes DA, Edwards GB: Bethanechol-responsive bladder atony in a colt foal after cystorrhaphy for cystorrhexis. *Vet Rec* 2000; 147:306-308.

Carr EA: Urinary incontinence. In Smith BP (ed): *Large Animal Internal Medicine*, 3rd edition, pp 836-838, St Louis, Mosby, 2002.

Gehlen H, Klug E: Urinary incontinence in the mare due to iatrogenic trauma. *Equine Vet Educ* 2001; 13:183-186.

Holt PE: Urinary incontinence in mature horses. *Equine Vet Educ* 1997; 9:85-88.

Ronen N: Measurements of urethral pressure profiles in the male horse. *Equine Vet J* 1994; 26:55-58.

Scarlat WK, Buechner-Maxwell VA, Karzenski S et al: Urinary incontinence and incoordination in three horses associated with equine protozoal myeloencephalitis. *J Equine Vet Sci* 1999; 19:642-645.

Sponseller BA, McElhaney R, Carlson GP et al: Frontal septation of the bladder in a mare. *J Vet Intern Med* 1998; 12:313-315.

Watson ED, McGorum BC, Keeling N et al: Oestrogen-responsive urinary incontinence in two mares. *Equine Vet Educ* 1997; 9:81-84.

CHAPTER 17.3

Congenital Disorders of the Urinary Tract

EMILY A. GRAVES

East Lansing, Michigan

Although congenital malformations of the equine urinary tract are rare, anomalies have been documented to affect all portions of the tract. Whereas some defects are revealed in neonatal foals, others are discovered incidentally at *post mortem* examination of mature horses. Abnormalities include ectopic ureters, patent urachus, renal agenesis/hypoplasia/dysplasia, polycystic kidneys and renal cysts, bladder defects, pendulant kidney, rectovaginal or rectourethral fistulas, ureteral defects, and vascular anomalies.

ECTOPIC URETER

Ectopic ureters result from abnormal embryologic development of the mesonephric and/or metanephric ducts and tissue. Specifically, ectopic ureters result from failure of the metanephric duct to (1) migrate cranially to the trigone of the bladder or (2) be incorporated into the urogenital sinus. Also, in fillies, failure of regression of the mesonephric duct(s) leads to opening of the ureter(s) into the uterus or vagina. In colts, the mesonephric ducts develop into the Wolffian duct system of the reproductive tract.

The most common clinical presentation is a filly with a lifelong history of urinary incontinence and concomitant hindlimb urine scalding. A true sex predilection has not been proven, but some studies suggest fillies are affected more commonly. This may represent the fact that normal

retrograde flow of urine in colts from the pelvic urethra to the bladder makes incontinence a less common complaint. Affected males tend to present with histories of chronic urinary tract infections.

Diagnosis relies on visual speculum examination in fillies; endoscopic examination of the urethra, bladder, and vagina (in fillies); and contrast radiography. Examination must determine if the condition is unilateral or bilateral. Endoscopy is often adequate in determination of the location of the ectopic ureteral opening. In addition, dye injection into the bladder or intravenously can identify the source of urine flow via endoscopy.

Occasionally, radiographic studies are required to localize the opening(s). Options include contrast retrograde cystography or urethrography, intravenous urography, and intravenous pyelography. The latter two options pose a challenge in older animals because adequate radiographic technique may not be achievable. These radiographic tests can provide useful detail of the upper urinary tract before surgery. Other important diagnostic tests are renal ultrasonography, complete blood count, chemistry profile, urinalysis, and urine culture. Using ultrasonography and/or radiography, common abnormalities found in association with ureteral ectopia include hydroureter and hydronephrosis on the affected side. Appropriate treatment for urinary tract infections must be completed before surgical intervention. Contralateral kidney function

or therapeutically, if urine culture yields a susceptible pathogen. Additionally, skin areas affected by urine leakage should be cleansed daily, dried thoroughly, and covered with zinc oxide ointment or petrolatum to prevent scalding. Treatment should be continued until the incontinence has resolved. Unfortunately, prognosis for horses with incontinence of neurogenic origin is usually poor, unless caused by a specific, potentially treatable or self-limiting neurologic disease such as EPM or EHV-1 encephalomyelopathy.

Supplemental Readings

Booth TM, Howes DA, Edwards GB: Bethanechol-responsive bladder atony in a colt foal after cystorrhaphy for cystorrhexis. *Vet Rec* 2000; 147:306-308.

Carr EA: Urinary incontinence. In Smith BP (ed): *Large Animal Internal Medicine*, 3rd edition, pp 836-838, St Louis, Mosby, 2002.

Gehlen H, Klug E: Urinary incontinence in the mare due to iatrogenic trauma. *Equine Vet Educ* 2001; 13:183-186.

Holt PE: Urinary incontinence in mature horses. *Equine Vet Educ* 1997; 9:85-88.

Ronen N: Measurements of urethral pressure profiles in the male horse. *Equine Vet J* 1994; 26:55-58.

Scarlat WK, Buechner-Maxwell VA, Karzenski S et al: Urinary incontinence and incoordination in three horses associated with equine protozoal myeloencephalitis. *J Equine Vet Sci* 1999; 19:642-645.

Sponseller BA, McElhaney R, Carlson GP et al: Frontal septation of the bladder in a mare. *J Vet Intern Med* 1998; 12:313-315.

Watson ED, McGorum BC, Keeling N et al: Oestrogen-responsive urinary incontinence in two mares. *Equine Vet Educ* 1997; 9:81-84.

CHAPTER 17.3

Congenital Disorders of the Urinary Tract

EMILY A. GRAVES

East Lansing, Michigan

Although congenital malformations of the equine urinary tract are rare, anomalies have been documented to affect all portions of the tract. Whereas some defects are revealed in neonatal foals, others are discovered incidentally at *post mortem* examination of mature horses. Abnormalities include ectopic ureters, patent urachus, renal agenesis/hypoplasia/dysplasia, polycystic kidneys and renal cysts, bladder defects, pendulant kidney, rectovaginal or rectourethral fistulas, ureteral defects, and vascular anomalies.

ECTOPIC URETER

Ectopic ureters result from abnormal embryologic development of the mesonephric and/or metanephric ducts and tissue. Specifically, ectopic ureters result from failure of the metanephric duct to (1) migrate cranially to the trigone of the bladder or (2) be incorporated into the urogenital sinus. Also, in fillies, failure of regression of the mesonephric duct(s) leads to opening of the ureter(s) into the uterus or vagina. In colts, the mesonephric ducts develop into the Wolffian duct system of the reproductive tract.

The most common clinical presentation is a filly with a lifelong history of urinary incontinence and concomitant hindlimb urine scalding. A true sex predilection has not been proven, but some studies suggest fillies are affected more commonly. This may represent the fact that normal

retrograde flow of urine in colts from the pelvic urethra to the bladder makes incontinence a less common complaint. Affected males tend to present with histories of chronic urinary tract infections.

Diagnosis relies on visual speculum examination in fillies; endoscopic examination of the urethra, bladder, and vagina (in fillies); and contrast radiography. Examination must determine if the condition is unilateral or bilateral. Endoscopy is often adequate in determination of the location of the ectopic ureteral opening. In addition, dye injection into the bladder or intravenously can identify the source of urine flow via endoscopy.

Occasionally, radiographic studies are required to localize the opening(s). Options include contrast retrograde cystography or urethrography, intravenous urography, and intravenous pyelography. The latter two options pose a challenge in older animals because adequate radiographic technique may not be achievable. These radiographic tests can provide useful detail of the upper urinary tract before surgery. Other important diagnostic tests are renal ultrasonography, complete blood count, chemistry profile, urinalysis, and urine culture. Using ultrasonography and/or radiography, common abnormalities found in association with ureteral ectopia include hydroureter and hydronephrosis on the affected side. Appropriate treatment for urinary tract infections must be completed before surgical intervention. Contralateral kidney function

can be assessed with bloodwork (BUN and creatinine), measurement of glomerular filtration rate (GFR), excretory urography, and nuclear scintigraphy.

Treatment options include surgical reimplantation of the ureter(s) into the bladder wall. Surgical techniques described include (1) submucosal tunneling of the ureter followed by establishment of a new ureteral opening near the trigone of the bladder and (2) side-to-side anastomosis of the ureter and dorsolateral bladder wall. In both instances, long-term concerns with ascending pyelonephritis remain for the life of the animal. With bilateral disease, a normal micturition response and adequate urethral sphincter competence should be documented before surgery. In addition, in cases of unilateral ectopia, unilateral nephrectomy is a proven, realistic treatment option. Normal contralateral kidney function is necessary. Several case reports describe the technique and showed successful outcomes. Major complications associated with these techniques are nonfunctional ureteral opening(s), hemorrhage, postoperative peritonitis, and adhesion formation.

PATENT URACHUS

In the fetus, the urachus serves as the connection from the bladder to the allantois and allows for passage of fetal urine accumulation. Normally, the urachus closes at birth and regresses to form a scar. In neonates, a patent urachus may be congenital or develop as a secondary complication in cases of failure of passive transfer or septicemia. The etiology of the congenital form is poorly understood. Multiple theories have been proposed, including an association with umbilical cord length or cord torsion. Patency secondary to omphalitis/omphalophlebitis is the most common scenario observed in foals. Clinical signs include urine leaking from the umbilicus sporadically and/or during micturition, persistently moist umbilicus, and pollakiuria. Septic foals must be monitored daily for signs of patent urachus (and ruptured bladder; see Chapter 12.6: "Neonatal Septicemia" and Chapter 17.13: "Uroperitoneum") using ultrasonography. Several reports exist of septic foals acquiring urachal patency despite several days or weeks of hospitalization and appropriate medical therapy.

Some clinicians suggest applying chemical agents topically to cauterize the patent urachal remnant. Options include dilute iodine or chlorhexidine solutions, concentrated phenol solution, or silver nitrate application. Although many breeding farms perform this treatment prophylactically, others have shown that these agents can be irritating to the umbilical stalk and surrounding skin and may potentiate the development of omphalitis. If the problem persists or umbilical infection is concurrently present, surgical resection is indicated. This procedure typically involves removal of the urachus and a small portion of the apex of the bladder.

RENAL AGENESIS, HYPOPLASIA, AND DYSPLASIA

Renal agenesis can be unilateral or bilateral. It is a consequence of failure of fusion of the metanephric duct to the metanephrogenic tissue in the fetus. Unilateral cases may be discovered incidentally in mature animals, particularly during reproductive tract exams, because many cases have concurrent genital tract anomalies. A bilateral condition

was described in a foal that had severe azotemia within hours of parturition and multiple additional urogenital system defects that were found at necropsy. With unilateral agenesis, clinical disease may become evident if the opposite kidney develops insufficiency, such as a nephrolith with associated hydronephrosis.

Renal hypoplasia is defined as total renal mass less than one third of normal or one kidney at least 50% smaller than normal. The defect itself results from reduced metanephrogenic tissue or from abnormal induction of nephron formation. Unilateral hypoplasia typically is found with hypertrophy of the opposite kidney and normal kidney function. Bilateral disease leads to chronic renal failure.

Renal dysplasia is described as disorganized renal tissue development secondary to abnormal differentiation, *in utero* ureteral obstruction (e.g., by polyps), fetal viral infection, or teratogen exposure. Clinical signs and bloodwork abnormalities include weight loss, depression, azotemia, hyponatremia, and hypochloremia. Affected kidneys generally have normal size, although they may become small and irregular as chronic renal failure progresses. Unilateral and bilateral diseases have been described. Histopathologic changes include small glomeruli and immature tubules without evidence of inflammation.

POLYCYSTIC KIDNEYS AND RENAL CYSTS

Polycystic kidney disease has been documented in several adult horses. An underlying mechanism has not been outlined, but many theorize that the disorder has a hereditary basis (based on human polycystic kidney syndromes). Equine cases present with signs of weight loss, hematuria, and/or anorexia. On examination, significantly enlarged kidneys can be palpated per rectum and azotemia may be documented. Ultrasonographic evaluation reveals multiple, variable-size cysts throughout the cortex and medulla. Based on work in human medicine, renal failure is thought to ensue as expanding cysts compress normal renal parenchyma. Also, changes in tubular basement membranes and epithelium may lead to tubular obstruction and further cyst formation. Documented equine cases have been bilateral and shown variable signs of chronic renal failure. Euthanasia was performed upon or several months after diagnosis.

Renal cysts may be found at necropsy incidentally and usually are associated with the cortex rather than the medulla. They have an unknown pathogenesis but are theorized to result from a basement membrane defect that leads to tubular dilatation. Congenital cysts are distinguished from acquired ones by the lack of associated fibrosis.

BLADDER HYPOPLASIA, AGENESIS, AND FUSION FAILURE

The prevalence of this condition is unknown. Foals present with signs of uroperitoneum, including depression, stranguria, bloated abdomen, hyponatremia, hypochloremia, and hyperkalemia. Although many are thought to result from trauma during parturition, some surgeons report finding full thickness, smooth-edged defects in the dorsal bladder wall at surgery. This suggests, in some cases, that the defect may be developmental, not traumatic, in origin. Specific anomalies reported in the literature include both

dorsal and ventral bladder wall defects. Surgical correction is the treatment of choice.

PENDULANT KIDNEY

Pendulant kidney is another rare anomaly in horses and generally is discovered incidentally during transrectal palpation. Transrectal palpation reveals a mobile kidney connected to the dorsal body wall by a thin piece of connective tissue. Potential clinical problems consist of ureteral obstructions caused by rotation of the affected kidney.

RECTOVAGINAL OR RECTOURETHRAL FISTULAS

Rectovaginal fistulas, affecting fillies only, and rectourethral fistulas result from failure of the urorectal fold to properly expand caudally during development to divide the hindgut and urogenital sinus. They are rare and tend to be associated with other developmental anomalies, including atresia ani, scoliosis, agenesis of the coccygeal vertebrae, and microphthalmia. Fistulas and concurrent defects can be repaired surgically under general anesthesia, but multiple procedures usually are needed. Because a hereditary component has not been ruled out, affected animals should not be used as breeding stock.

URETERAL DEFECTS

Signs of ureteral defects include uroperitoneum and/or urine accumulation in the retroperitoneal space. Unilateral and bilateral conditions have been documented. Proposed causes are developmental defect or traumatic tearing. Abdominal ultrasound and excretory urography can be combined to diagnose uroperitoneum and then to localize the defect(s), respectively. In most cases, however, the defect is localized during celiotomy as foals diagnosed with uroperti-

toneum are taken to surgery in lieu of completing further diagnostic tests. At surgery, ureteral catheterization via cystotomy followed by retrograde injection of methylene blue can identify the defect site. Subsequent suturing of the defect around the indwelling catheter has been performed successfully in two published cases.

VASCULAR ANOMALIES

Abnormal vascular supply to the urinary tract is rare. Clinical signs include partial ureteral obstruction, hydronephrosis, hematuria, hemoglobinuria, and colic. Anomalies can be extrarenal or intrarenal (also called *renal arteriovenous malformations*). An aortic aneurysm and associated arterioureteral fistula were described in a colt. Intrarenal problems may not cause clinical signs in the young animal. The vessels tend to be enlarged and tortuous. Hematuria and hemoglobinuria are thought to occur when abnormal vessels are in proximity to the collecting tubules.

Diagnostic tests should focus on determination of what level of the tract is affected and if the disorder is unilateral or bilateral. If the malformation is unilateral and opposite kidney function is normal, nephrectomy on the affected side should be recommended. In addition, renal embolization to prevent fatal hematuria has been performed. Conservative management is another option in those cases with mild clinical signs.

Supplemental Readings

- Richardson DW: Urogenital problems in the neonatal foal. *Vet Clin North Am Equine Pract* 1985; 1:179-188.
Schott HC: The urinary system, developmental malformations of the urinary tract. In Reed SM, Bayly WM (eds): *Equine Internal Medicine*, Philadelphia, WB Saunders, 1998.

CHAPTER 17.4

Differential Diagnosis of Polyuria/Polydipsia

DEREK C. KNOTTENBELT
Liverpool, United Kingdom

Polyuria/polydipsia (PU/PD) is an important clinical sign that usually indicates failure of normal homeostatic mechanisms that control water balance. A horse with urine output of more than 50 ml/kg/day and water intake of more than 100 ml/kg/day is classified as a case of the PU/PD. In a 500-kg horse, this equates to pro-

duction of 25 L of urine and consumption of 50 L of water over a 24-hour period. The underlying primary pathophysiology may be either an increased water intake or an increased urine output. Owners may be misled and report either excessive or reduced water intake and/or urine production but, without measurements, confirmation of the

dorsal and ventral bladder wall defects. Surgical correction is the treatment of choice.

PENDULANT KIDNEY

Pendulant kidney is another rare anomaly in horses and generally is discovered incidentally during transrectal palpation. Transrectal palpation reveals a mobile kidney connected to the dorsal body wall by a thin piece of connective tissue. Potential clinical problems consist of ureteral obstructions caused by rotation of the affected kidney.

RECTOVAGINAL OR RECTOURETHRAL FISTULAS

Rectovaginal fistulas, affecting fillies only, and rectourethral fistulas result from failure of the urorectal fold to properly expand caudally during development to divide the hindgut and urogenital sinus. They are rare and tend to be associated with other developmental anomalies, including atresia ani, scoliosis, agenesis of the coccygeal vertebrae, and microphthalmia. Fistulas and concurrent defects can be repaired surgically under general anesthesia, but multiple procedures usually are needed. Because a hereditary component has not been ruled out, affected animals should not be used as breeding stock.

URETERAL DEFECTS

Signs of ureteral defects include uroperitoneum and/or urine accumulation in the retroperitoneal space. Unilateral and bilateral conditions have been documented. Proposed causes are developmental defect or traumatic tearing. Abdominal ultrasound and excretory urography can be combined to diagnose uroperitoneum and then to localize the defect(s), respectively. In most cases, however, the defect is localized during celiotomy as foals diagnosed with uroperti-

toneum are taken to surgery in lieu of completing further diagnostic tests. At surgery, ureteral catheterization via cystotomy followed by retrograde injection of methylene blue can identify the defect site. Subsequent suturing of the defect around the indwelling catheter has been performed successfully in two published cases.

VASCULAR ANOMALIES

Abnormal vascular supply to the urinary tract is rare. Clinical signs include partial ureteral obstruction, hydronephrosis, hematuria, hemoglobinuria, and colic. Anomalies can be extrarenal or intrarenal (also called *renal arteriovenous malformations*). An aortic aneurysm and associated arterioureteral fistula were described in a colt. Intrarenal problems may not cause clinical signs in the young animal. The vessels tend to be enlarged and tortuous. Hematuria and hemoglobinuria are thought to occur when abnormal vessels are in proximity to the collecting tubules.

Diagnostic tests should focus on determination of what level of the tract is affected and if the disorder is unilateral or bilateral. If the malformation is unilateral and opposite kidney function is normal, nephrectomy on the affected side should be recommended. In addition, renal embolization to prevent fatal hematuria has been performed. Conservative management is another option in those cases with mild clinical signs.

Supplemental Readings

- Richardson DW: Urogenital problems in the neonatal foal. *Vet Clin North Am Equine Pract* 1985; 1:179-188.
- Schott HC: The urinary system, developmental malformations of the urinary tract. In Reed SM, Bayly WM (eds): *Equine Internal Medicine*, Philadelphia, WB Saunders, 1998.

CHAPTER 17.4

Differential Diagnosis of Polyuria/Polydipsia

DEREK C. KNOTTENBELT
Liverpool, United Kingdom

Polyuria/polydipsia (PU/PD) is an important clinical sign that usually indicates failure of normal homeostatic mechanisms that control water balance. A horse with urine output of more than 50 ml/kg/day and water intake of more than 100 ml/kg/day is classified as a case of the PU/PD. In a 500-kg horse, this equates to pro-

duction of 25 L of urine and consumption of 50 L of water over a 24-hour period. The underlying primary pathophysiology may be either an increased water intake or an increased urine output. Owners may be misled and report either excessive or reduced water intake and/or urine production but, without measurements, confirmation of the

extent of the problem often is difficult. Although important pathologic causes exist for the PU/PD syndrome, significant physiologic and behavioral causes also exist. The major causes of PU/PD in horses include renal failure, pituitary adenoma (Cushing's disease), and primary or "psychogenic" polydipsia. Less frequent causes include excessive salt consumption, central and nephrogenic diabetes insipidus, diabetes mellitus, sepsis and/or endotoxemia, and iatrogenic causes (for example, sedation with α_2 -adrenergic agonists, corticosteroid therapy, or diuretic use).

WATER INTAKE AND URINE PRODUCTION

Water consumption and urine production vary with age, diet, workload, environmental temperature, and gastrointestinal water absorption. The normal water maintenance requirements have been estimated at 40 to 60 ml/kg/day. Water requirements are proportional to metabolic body size, so a Shire horse requires relatively less water per kilogram body weight than a Shetland pony. Fat animals also appear to require less water than lean ones. Environmental conditions influence water intake significantly. Animals maintained in higher ambient temperatures drink more than those in cold places.

Although urination is the most obvious means of fluid loss, it is not responsible for the major losses; rather urine production provides the fine controlling mechanism for water and electrolyte homeostasis. The volume of urine produced varies between 15 and 30 ml/kg/day. Dietary composition affects the amount of urine produced. For example, pelleted dry feeds and legume hay result in higher urine output than does grass hay. Diets with a high salt content encourage drinking and increase the volume of urine produced. Horses undertaking heavy exercise, those stabled in hot climates, and those with diarrhea may have a water intake in excess of 100 L per day yet produce normal volumes of urine.

Urine is produced by filtration of blood within the glomerulus and modification of the filtrate in the renal tubules. Reabsorption of water is dependent on maintenance of renal interstitial hypertonicity and the action of antidiuretic hormone (ADH). ADH exerts its effect by increasing the permeability of the collecting ducts to water. Normally, about 80% of the glomerular filtrate has been reabsorbed by the time it reaches the distal tubules; therefore with normal renal function, only 20% of water is subject to the action of ADH.

The renin-angiotensin system is a second hormonal mechanism involved in water regulation. During hypovolemia, renin is released from the juxtaglomerular cells of the kidney and initiates the conversion of angiotensin-I to angiotensin-II. This decreases renal blood flow and also stimulates production of aldosterone from the adrenal cortex. Aldosterone in turn has a direct action on the renal tubules, which causes the conservation of sodium ions and water and the selective excretion of potassium ions.

DIAGNOSTIC APPROACH TO POLYURIA/POLYDIPSIA

Veterinary practitioners must decide whether the problem is the result of polyuria or polydipsia. A thorough clinical examination and detailed history is obligatory; these might

provide much important information. The physiologic causes for increased thirst and urination must be differentiated from pathologic causes. In many cases, either the polydipsia or the polyuria is pathologic and the changes in the other could be viewed as secondary physiologic effects. Thus a horse that produces dilute urine in large volumes as result of pathologic renal failure has increased water intake as a secondary physiologic response to the water loss. Similarly, a horse with psychogenic polydipsia has increased urine output. Figure 17.4-1 is a clinical flow chart that will help to identify the major causes of PU/PD.

History

A history may be sufficient to eliminate some of the behavioral and physiologic factors responsible for PU/PD and to identify the secondary effects of medications. The duration of the problem should be established and changes in management or feeding identified. Any previous medical history suggestive of Cushing's disease (e.g., atypical laminitis and failure to shed hair in spring and summer) should be noted. Many horse owners have difficulty distinguishing polyuria from pollakiuria (frequent urination). The latter may be caused by cystitis, vaginitis, metritis, and estrous behavior. The animal playing with its water bucket also may cause excessive stall wetting.

Clinical Examination

A complete clinical examination should be performed. Although few single pathognomonic signs exist of most conditions responsible for PU/PD, several abnormalities taken together may make the diagnosis much clearer. Hydration status should be estimated so that any concurrent azotemia can be evaluated in light of hydration. A rectal examination of the palpable regions of the urinary tract often is helpful and its diagnostic value can be enhanced by transrectal and transabdominal ultrasonography of the kidneys and ureters. The horse should be confined to its stall for 24 hours and its water intake measured. If possible, urine production also should be measured with a suitable collection device. A normal horse on a hay diet produces 5 to 15 L of urine per day.

A complete blood count and biochemistry profile should be performed. Indications of chronic inflammation in the complete blood count coupled with azotemia and isosthenuria may indicate the presence of chronic renal failure, especially if hypercalcemia and hypophosphatemia are also present. Analysis of freely voided urine is also important. Leukocytes in the urine can indicate the presence of pyelonephritis. Glycosuria coupled with hyperglycemia suggests the presence of Cushing's disease or diabetes mellitus.

Water Deprivation Test

This test assesses the ability of the renal tubules to respond to ADH. In the absence of azotemia, dehydration, or hyperglycemia, the test helps to differentiate between central and nephrogenic diabetes insipidus and psychogenic polydipsia. Water deprivation should be done only after renal failure has been ruled out as a cause of PU/PD. The horse must be weighed and a urine sample obtained. The horse is confined without access to water and urine samples are collected as

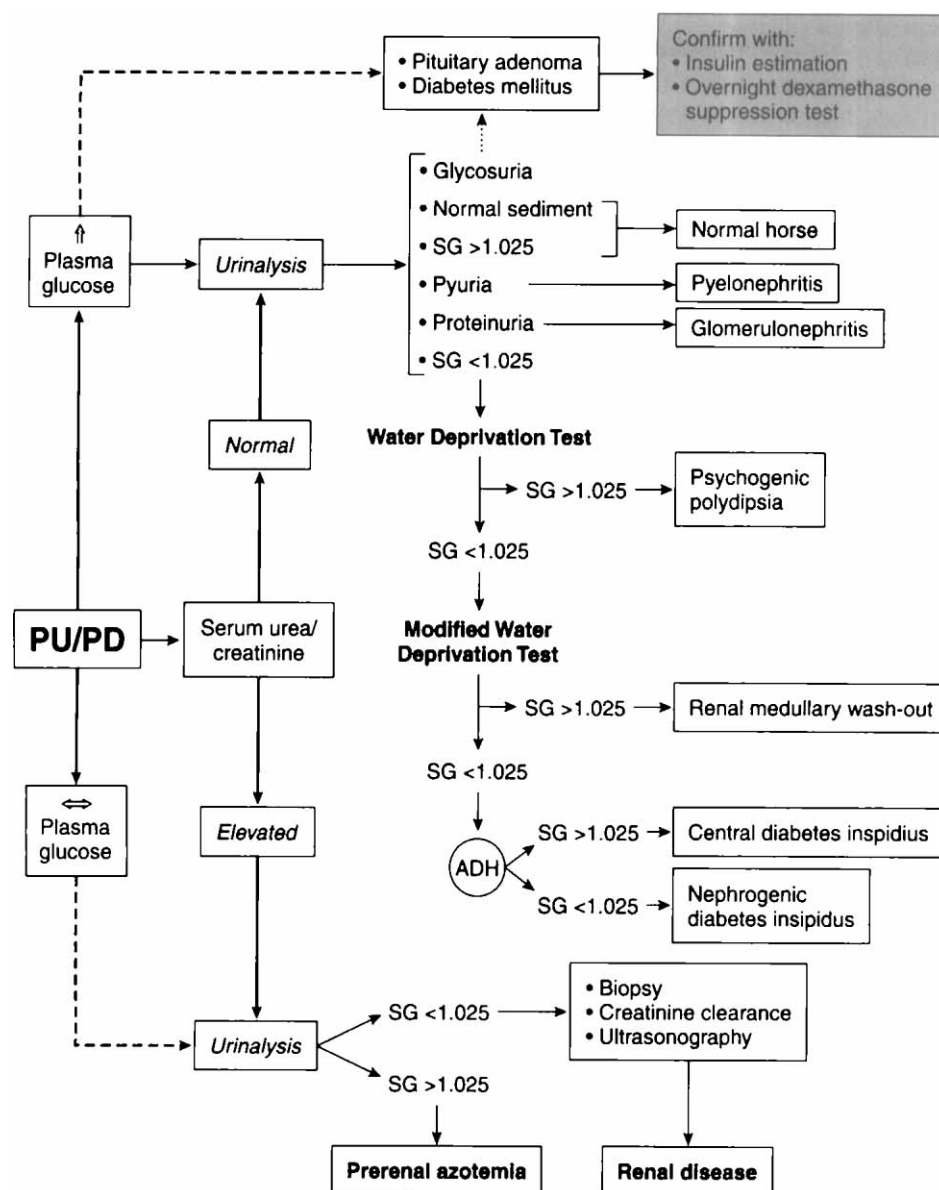


Figure 17.4-1 A clinical flow chart to identify the major causes of polyuria/polydipsia. SG, Specific gravity; ADH, antidiuretic hormone.

often as practicable. The test continues until a specific gravity of the urine exceeds 1.025 or the horse loses 5% of its body weight, whichever comes first.

The water deprivation test has been modified for use in practice situations. Water intake is restricted to 40 ml/kg/day for up to 4 days. This should result in urinary concentration, even in cases of psychogenic polydipsia that have resulted in washout of electrolytes from the renal medulla.

Desmopressin Response Test

If a modified water deprivation test fails to induce urinary concentration after 4 days, the diagnosis of diabetes insipidus can be made. Intravenous administration of 20 µg of desmopressin acetate (DDAVP, equal in antidiuretic activity to 80 IU of ADH) enables a clinician to differentiate between

central and nephrogenic forms of the disease. If the urine concentrates in response to DDAVP, the diabetes is of central origin but if it does not, it is likely to be nephrogenic.

POLYDIPSIA

Polydipsia may be physiologic or pathologic. The physiologic increases in water intake can occur when the animal is on a dry, salty, low-residue diet, or after exercise.

Psychogenic Polydipsia

Psychogenic polydipsia is one of the most common causes of PU/PD in adult, stabled horses. It often occurs in young animals and is considered a vice associated with boredom. Often management or environment has changed. Dietary

factors also are implicated as a cause. These include sustained high intake of dry matter and excessive or compulsive salt intake.

Psychogenic polydipsia is associated with the most severe form of polydipsia and polyuria. Affected animals are usually in good body condition and have no biochemical evidence of renal failure, although the urine is invariably hyposthenuric with a low specific gravity (<1.005). Horses with a short history of this condition commonly are able to concentrate the urine in response to water deprivation but longstanding cases have no such ability. This possibly is due to washout of electrolytes from the renal medulla and loss of the normal osmotic gradients responsible for urinary concentration.

If no evidence exists of renal failure, a water deprivation test should be performed. If urinary concentration does not occur, the modified water deprivation test should then be performed. By the end of this test, the horse with renal medullary washout has restored the normal osmotic gradients and produces urine with a specific gravity of more than 1.025.

Treatment of psychogenic polydipsia involves alteration of management and environment to relieve boredom. The routine for feeding and bedding should be changed and the horse should be given more exercise by turning out in a paddock, use of a hot-walker, or being ridden. Water intake should be restricted to a maximum of 40 ml/kg/day for 2 to 4 days to restore the electrolyte gradient within the kidney.

High Ambient Temperature

Loss of fluid through sweat and the respiratory system stimulates thirst. Some horse owners may identify the increased water intake associated with high environmental temperatures as polydipsia. However, under these conditions, many horses are affected with the so-called problem.

Compulsive Salt/Glucose Consumption

Although it is a rare event, some horses may attack the salt or glucose block and bite large chunks of the solid material. Clinical history is usually clear, although reasons behind the vice are usually much less so. Diarrhea may develop as a result of osmotic fluid retention within the intestine. An abnormally high fractional excretion of sodium is detected if salt ingestion is abnormally high. Excessive glucose ingestion usually produces a significant and prolonged glycosuria for up to 4 to 6 hours.

POLYURIA

Diabetes Mellitus

Diabetes mellitus resulting from loss of pancreatic islet cells is extremely rare in horses but may be induced by parasitic migration. In cases of diabetes mellitus, polyuria is the result of osmotic diuresis resulting from the glycosuria. At the same time, polydipsia occurs because of dehydration or increased osmolality of plasma. The majority of horses that exhibit hyperglycemia and glycosuria have dysfunction of the pars intermedia of the pituitary gland (Cushing's disease).

Diabetes Insipidus

Diabetes insipidus of central origin arises from failure of the pars distalis of the pituitary gland to produce ADH. It can be secondary to viral encephalomyelitis or to compression of the pituitary gland as part of the Cushing's disease syndrome. Nephrogenic diabetes insipidus is caused by a lack of tubular response to ADH. It can be a familial condition, can be secondary to acute renal bacterial infections, and can be associated with drug therapy, obstructions of the urinary tract, and neoplastic disorders.

Cushing's Disease

Cushing's disease (see Chapter 16.2: "Pituitary Pars Intermedia Dysfunction: Equine Cushing's Disease"), attributable to dysfunction of the pars intermedia of the pituitary gland, is accompanied by a loss of diurnal cortisol rhythmicity. The persistent increase in plasma cortisol concentration gives rise to an increase in glomerular filtration rate and causes hyperglycemia, both of which may induce polyuria.

Sepsis and Endotoxemia

Prostaglandin E_2 , produced in response to endotoxin, has a powerful vasodilator effect on the renal blood vessels and also reduces the sensitivity of the renal collecting tubules to ADH. Urine production may increase even though significant dehydration may occur.

Iatrogenic Causes of Polyuria

Administration of large volumes of intravenous fluids can result in production of large volumes of urine. Exogenous corticosteroid administration also may cause polyuria, although the mechanism remains unclear. Horses that receive prolonged medication with dexamethasone may show profound glycosuria (20 to 30 grams per liter), which inevitably leads to osmotic diuresis. A transient diuresis accompanies sedation with the α_2 -adrenoreceptor agonist drugs xylazine and detomidine. Although these agents also cause transient hyperglycemia and occasionally glycosuria, the more likely mechanism of the polyuria is antagonism of the action of ADH by activation of α_2 -adrenoreceptors on the collecting duct epithelial cells.

Supplemental Readings

- Brown CM: Polyuria. In Robinson NE (ed): *Current Therapy in Equine Medicine*, 4th edition, pp 486-488, Philadelphia, WB Saunders, 1997.
- Buntain BJ, Coffman JR: Polyuria and polydipsia in a horse induced by psychogenic salt consumption. *Equine Vet J* 1981; 13:266-268.
- Haupt KA: Thirst in horses: the physiological and psychological causes. *Equine Pract* 1987; 9:28-30.
- Love S: Equine Cushing's disease. *Br Vet J* 1993; 149:139-153.
- Schott HC: Polyuria and polydipsia. In Reed SM, Bayly WM (eds): *Equine Internal Medicine*, pp 895-901, Philadelphia, WB Saunders, 1998.
- Schott HC, Bayly WM, Reed SM et al: Nephrogenic diabetes insipidus in sibling colts. *J Vet Intern Med* 1993; 7:68-72.

CHAPTER 17.5

Obstructive Disease of the Urinary Tract

KATJA F. DÜSTERDIEK
Blacksburg, Virginia

The majority of cases of urinary tract obstruction are caused by urolithiasis. Other causes include trauma, neoplasia, and urinary tract displacement. The prevalence of urolithiasis is estimated at 0.11%, and 7.8% of horses examined for urinary tract disease were diagnosed with urinary calculi. Urolithiasis is more common in males than in females. A lower prevalence in female horses has been attributed to the shorter and more distensible urethra of the mare, which allows for voiding of uroliths. The majority of calculi are located within the urinary bladder, but they also can occur within kidneys or ureters, followed by the urethra. Urinary calculi were found in more than one site in about 9% of horses in a retrospective study.

Factors believed to contribute to urolith formation include trauma to the urinary tract lining, supersaturation of urine with certain minerals, and urine stasis or prolonged urine retention. Imbalances of substances that inhibit or promote crystal growth and genetic predisposition to excrete larger amounts of calcium, uric acid, or oxalates in urine likely contribute further to formation of uroliths. Equine urine normally is supersaturated with calcium carbonate, but it is also rich in mucus, a natural inhibitor of crystal growth. Therefore it is surprising that urolithiasis is not more common in horses.

Tissue damage is believed to be the most important factor for development of urolithiasis in horses. In general, nucleation is the first step for formation of a calculus. Minerals are deposited around a nidus such as necrotic tissue, desquamated cells, or leukocytes, followed by slow and continuous crystal growth.

Two basic forms of uroliths exist in horses. The more common form is yellow-green, with a spiculated surface; it is broken down easily. Less commonly, uroliths are gray, smooth, and more resistant to fragmentation. Most equine urinary calculi are primarily composed of calcium carbonate with occasional addition of phosphate or struvite.

Clinical signs of urolithiasis vary and depend on site and degree of obstruction. The most commonly observed sign is poor body condition. Other signs include gross or microscopic hematuria, tenesmus, colic, and pollakiuria, dysuria, or incontinence and urine scalding of the rear limbs. Horses with urinary calculi can present with normal serum chemistry values or with azotemia, hyperkalemia, hyponatremia, hypercalcemia, and hypophosphatemia. Urinalysis may show proteinuria, microscopic hematuria, and pyuria.

NEPHROLITHIASIS AND URETEROLITHIASIS

Nephrolithiasis and ureterolithiasis are described rarely, but their occurrence should not be overlooked. In a review of 68 horses with urolithiasis, 25% had uroliths in the kidneys or ureters. Further, some horses with cystic calculi had additional calculi in the upper urinary tract. Nephroliths may develop around a nidus associated with a variety of renal diseases, which include pyelonephritis, renal tubular or papillary necrosis, and neoplasia. It has been speculated that racehorses are at greater risk for this disease because of the common use of nonsteroidal anti-inflammatory drugs and the associated risk of papillary necrosis in these horses.

Horses with nephrolithiasis or ureterolithiasis often remain asymptomatic until bilateral obstructive disease results in acute or chronic renal failure. Nonspecific signs of uremia such as poor performance, inappetence, lethargy, and weight loss are observed more commonly than signs of obstructive disease, including colic, stranguria, and hematuria. Rectal palpation may reveal an enlarged kidney or ureter and in some instances the calculus can be palpated in the enlarged ureter.

The diagnosis is made based on rectal and transcutaneous ultrasonographic examination findings. Calculi are detected as hyperechoic structures with a strong anechoic shadow. Small stones may be missed on ultrasonographic examination, but other findings such as dilation of the renal pelvis, proximal ureters, or hydronephrosis support upper urinary tract obstruction. Because infection often accompanies urolithiasis, a quantitative urine culture should be performed in all cases.

Most horses are in chronic renal failure at the time of diagnosis of upper urinary tract lithiasis. Surgical treatment does not seem to improve moderate or severe azotemia; therefore few cases are amenable to treatment. Treatment includes nephrectomy, nephrotomy, or ureterolithectomy.

Less invasive treatments have been attempted in more recent years. A distal ureteral calculus was removed using a basket stone dislodger (Dormia Stone Dislodger, V. Mueller, Division of American Hospital Supply, McGaw Park, Ill.) through a vestibulourethral approach in a mare. Electrohydraulic lithotripsy through a ureteroscope has been used successfully in a horse with a single unilateral ureterolith. A more recent means of upper urinary tract stone removal is extracorporeal shock wave lithotripsy

(ESWL). This technology has proven efficacious in the treatment of human nephrolithiasis. It uses a reflector to focus the energy from a shock wave created outside the body on a calculus located in the kidney. To this author's knowledge, this technology has not been used to treat equine upper urinary tract lithiasis.

CYSTIC CALCULI

Cystic calculi are the most commonly recognized type of equine uroliths. Most cystic calculi are flattened sphere-shaped stones with a spiculated surface, but smooth calculi or an accumulation of crystalloid sludge, termed *sabulous urolithiasis*, also can occur. The latter form usually develops as a result of bladder paralysis.

Clinical Signs

Cystic calculi interfere with normal urination. Thus clinical signs include hematuria, stranguria, pollakiuria, pyuria, and incontinence. Less commonly, signs of mild colic, tenesmus, vocalization, urine scalding, and loss of condition can be observed. Most cystic calculi are detected as a firm, round mass in the urinary bladder on rectal palpation. To facilitate palpation of the stone, emptying the bladder by transurethral catheterization may be necessary. This also allows assessment of patency of the urethra and collection of urine samples for urinalysis and quantitative culture. A transrectal ultrasonographic exam or cystoscopy can be used to confirm the diagnosis. Cystoscopy also provides a means to assess the severity of damage to the bladder mucosa and the functionality of both ureters. Further assessment of the upper urinary tract for evidence of urolithiasis is important because calculi may be found in multiple sites in the urinary tract. A complete blood count and serum biochemistry profile should be performed to document possible anemia, inflammation, or azotemia.

Treatment

Several different surgical techniques have been described for removal of cystic calculi in horses. The appropriate approach should be chosen based on the gender and temperament of the horse, familiarity of the surgeon with the approach, availability of facilities and instrumentation, and economics. Large cystic calculi have been approached via laparocystotomy, laparoscopic cystotomy, subischial urethrotomy, or pararectal cystotomy (Gökel's operation). Further, a number of means for stone fragmentation (lithotripsy) have been used, including surgical forceps, manual lithotrites, electrohydraulic lithotripsy, ballistic lithotripsy, and laser lithotripsy.

Laparocystotomy has been advocated as the treatment of choice for large cystic calculi in male horses. This approach allows removal of the stone without the need for fragmentation. With this approach, the urethra is not traumatized and a thorough evacuation of debris and smaller stone fragments is possible. However, general anesthesia is required and exposure of the bladder is difficult and can be inadequate in some cases. Postoperative recovery time is 9 to 12 weeks and potential complications

include peritonitis, bladder leakage, incisional infection, and dehiscence of the abdominal incision.

Laparoscopic cystotomy provides excellent exposure and visualization of the equine urinary bladder in addition to decreased patient morbidity and recovery time when compared with laparocystotomy. Disadvantages are the cost of specialized equipment and the necessity for familiarity of the surgeon with advanced laparoscopic procedures and suturing techniques.

Subischial urethrotomy can be performed as a standing procedure if the horse's temperament is suitable. The recovery time is considerably shorter than with laparocystotomy. A disadvantage of this approach is the potential for stricture or formation of a diverticulum at the urethrotomy site, in addition to the fact that in male horses most cystic calculi need to be fragmented. In contrast, the mare's urethra often permits manual removal without fragmentation of the calculus. The urethra is gently dilated manually, or a urethro-sphincterotomy is performed.

The use of surgical forceps or manual lithotrites to fragment calculi can be time consuming and frustrating, and it results in considerable trauma to the urethra, urinary bladder, and surrounding structures. The occurrence of a grade 3 rectal tear has been described with this technique. Other complications include perforation of the pelvic urethra or urinary bladder, peritonitis, orchitis, tenesmus, and dysuria. Commonly, the procedure is performed without endoscopic guidance and complete evacuation of debris and fragments of the calculus may not be achieved. This could contribute to an increased recurrence of cystic calculi.

Electrohydraulic lithotripsy through the urethra in a mare or through a subischial urethrotomy in males has been performed successfully under general anesthesia. An electrohydraulic lithotriptor uses the conversion of electrical energy into mechanical energy to create a shock wave of sufficient energy to fragment solid objects. The calculus can be fragmented atraumatically under direct observation through a rigid endoscope. Disadvantages of this technique are expense of the equipment and possible damage to the bladder wall if the probe is discharged when in contact with the mucosa.

Ballistic shock wave lithotripsy has been performed in anesthetized and standing animals under direct endoscopic guidance through a rigid endoscope. Lithotripsy is performed with a rigid probe that functions similarly to a pneumatic hammer. It transfers mechanical energy onto the calculus by direct contact with the stone. Soft tissue damage does not occur with this technique because heat is not produced during application of the probe. Further, the elastic nature of the bladder wall prevents direct mechanical trauma to the mucosa. Stabilization of the calculus during the procedure appears to be difficult and can be obtained via rectal or transurethral manual fixation. Disadvantages of the technique include expense and availability of the specialized equipment, in addition to the possibility for trauma to the rectum during manual stabilization of the calculus.

Laser lithotripsy provides another means of urinary calculus fragmentation. Two different types of lasers have been used for lithotripsy of equine urinary calculi: a flashlamp tunable dye laser (pulsed dye laser), and a holmium:yttrium-aluminum-garnet laser (Ho:YAG laser).

Both lasers are used in conjunction with a conventional flexible endoscope, allowing for observation of the procedure, resulting in efficient and atraumatic fragmentation of the calculus. The laser energy is delivered to the calculus via a flexible optical fiber, which is advanced through the biopsy channel of the endoscope. The pulsed dye laser appeared to be superior to the Ho:YAG laser in one report for fragmentation of a cystic calculus and similar observations have been made by others. However, lithotripsy with the Ho:YAG laser in humans is 90% to 100% successful, and reasons for slow fragmentation or failure to fragment calculi in horses could include differences in calculus composition, crystal structures, and gross texture.

The pulsed dye laser fragments calculi via photoacoustic effect. It fragments the calculus into 1- to 3-mm particles that can be removed readily via lavage. The pulsed dye laser has a low risk of soft tissue damage and is safely applicable throughout the urinary tract. Successful fragmentation of bladder calculi and a urethral calculus have been reported. The Ho:YAG laser causes fragmentation primarily via photothermal effect. It exerts its fragmentation effect on the calculus by drilling through it and produces smaller dustlike particles. The laser energy is absorbed by water, and therefore soft tissue damage is encountered only if the laser is discharged while it comes into contact with the mucosa.

The Ho:YAG laser is a versatile laser. It is used for lithotripsy and soft tissue surgery in humans. Fragmentation of equine cystic calculi and a urethral calculus by the Ho:YAG laser with and without additional help of a lithotrite or other crushing forceps has been achieved. However, in this author's experience lithotripsy of urinary calculi with this laser can be time consuming and could result in failure to fragment.

The disadvantage of laser lithotripsy is obviously the expense and availability of the equipment. However, leasing a laser (expected cost \$1000-\$1500) is possible, with a total cost of treatment comparable with that of laparocystotomy.

Pararectal cystotomy (Gökel's operation), in this author's opinion, should be considered only as a last resort in cases with economic constraints. Possible complications include pelvic abscessation and peritonitis if communication of the dissection plane with the peritoneal cavity occurs.

About 41% of horses treated for urolithiasis have recurrence of the problem. The use of urinary acidifiers may help to prevent recurrences. Further, decreasing dietary calcium intake by avoiding alfalfa hay and calcium supplements may be beneficial. Addition of 50 to 75 g salt to the daily diet may increase water intake and promote diuresis. The most effective way to prevent recurrence is elimination of urinary tract infections and complete evacuation of debris and stone fragments from the urinary tract.

URETHRAL CALCULI

Urethral calculi are primarily seen in male horses. In the absence of predisposing primary disease within the urethra, urethral calculi are usually small cystic calculi that have been passed into the urethra. The most common site for calculi to lodge is where the urethra narrows and passes over the ischial arch.

An obstructing calculus should be considered in a horse with signs of colic and frequent attempts to urinate. Some horses have blood on the urethral orifice. Palpation of the penis may reveal rhythmic contractions of the urethra and the calculus may be felt as a firm mass within the urethra. Rectal palpation reveals a filled, turgid bladder. The diagnosis is confirmed by passage of a urethral catheter or a flexible endoscope to the site of obstruction. Once rupture of the bladder occurs, horses show signs of depression and anorexia resulting from progressive electrolyte imbalances and azotemia. Rupture of the urinary bladder can be confirmed by comparing creatinine concentration of abdominal fluid with serum creatinine concentration. A twofold or greater increase of creatinine in peritoneal fluid over serum creatinine is considered diagnostic.

Calculi lodged in the urethra can be removed under general anesthesia through a ventral urethrotomy or, in the standing sedated horse, via transurethral laser lithotripsy. Calculi in the distal urethra have been removed by careful crushing of the stone with a hand or with forceps. Of concern is the degree of trauma to the urethra and resulting stricture. However, mucosal damage typically resolves without serious complications. Postoperatively, horses are treated with nonsteroidal antiinflammatory drugs and antibiotics until normal urination occurs.

Supplemental Readings

- Adams SB, Fessler JF: Perineal urethrotomy and removal of cystic calculi. In Adams SB, Fessler JF (eds): *Atlas of Equine Surgery*, Philadelphia, WB Saunders, 2000.
- Eustace RA, Hunt JM, Brearley MJ: Electrohydraulic lithotripsy for the treatment of cystic calculus in two geldings. *Equine Vet J* 1988; 20:221-223.
- Howard RD, Pleasant RS, May KA: Pulsed dye laser lithotripsy for treatment of urolithiasis in two geldings. *J Am Vet Med Assoc* 1998; 212:1600-1603.
- Koenig J, Hurtig M, Pearce S et al: Ballistic shock wave lithotripsy in an 18-year-old thoroughbred gelding. *Can Vet J* 1999; 40:185-186.
- Lavery S, Pascoe JR, Ling GV et al: Urolithiasis in 68 horses. *Vet Surg* 1992; 21:56-62.
- MacHarg MA, Foerner JJ, Phillips TN et al: Electrohydraulic lithotripsy for treatment of a cystic calculus in a mare. *Vet Surg* 1985; 14:325-327.
- May KA, Pleasant RS, Howard RD et al: Failure of holmium:yttrium-aluminum-garnet laser lithotripsy in two horses with calculi in the urinary bladder. *J Am Vet Med Assoc* 2001; 219:957-961.
- McIlwraith CW, Robertson JT: Removal of cystic calculi (laparocystotomy). In McIlwraith CW, Robertson JT (eds): *McIlwraith and Turner's Equine Surgery: Advanced Techniques*, 2nd edition, Baltimore, Williams & Wilkins, 1998.
- Ragle CA: Laparoscopic removal of cystic calculi. In Fischer AT (ed): *Equine Diagnostic and Surgical Laparoscopy*, Philadelphia, WB Saunders, 2001.
- Schott HC: Obstructive diseases of the urinary tract. In Reed SM, Bayly WM (eds): *Equine Internal Medicine*, Philadelphia, WB Saunders, 1998.
- Schumacher J, Schumacher J: Surgical management of urolithiasis in the equine male. In Wolfe DE, Moll HD (eds): *Large Animal Urogenital Surgery*, 2nd edition, Baltimore, Williams & Wilkins, 1998.

CHAPTER 17.6

Urinary Tract Neoplasia

CORNELIS JAN CORNELISSE

East Lansing, Michigan

PPrimary neoplasms of the urinary tract in the horse are rare and affect the kidneys, bladder, and external genitalia. Tumors of the ureters and urethra have not been reported except as a consequence of invasion by carcinomas from the renal pelvis and penis, respectively.

KIDNEYS

The most frequently reported renal neoplasm of the horse is the adenocarcinoma, which originates from the proximal convoluted tubules. Less common malignancies include renal pelvis carcinomas, nephroblastoma (Wilms' tumor), anaplastic carcinoma, and hemangiosarcoma. Overall, renal neoplasms are rare, with a prevalence of 0.11% to 0.16% among horses subjected to necropsy. They are almost always unilateral with left and right kidney equally affected, and no gender or breed predisposition is evident. The age range spans 4 to 22 years, although nephroblastomas have been reported only in young horses.

Clinical Signs and Diagnosis

The most common presenting complaint is weight loss, with hematuria and/or low-grade recurrent colic as additional signs. In almost all cases, a large firm mass is palpable on rectal examination. Because the signs can be so nonspecific, their duration in some cases has been reported for up to 18 months before the neoplasm has been diagnosed. Transabdominal ultrasound usually reveals a mass with multiple hyperechogenic, isoechogenic and anechogenic areas originating from a kidney. Often the mass exceeds the original size of the kidney and no recognizable renal tissue can be detected.

The most commonly reported laboratory abnormality is a low-grade anemia and a mild neutrophilia. Additionally mild prolongation of coagulation times, mild elevations in liver enzymes, and azotemia have been found in advanced stages of the disease. Anaplastic renal carcinoma has been associated with recurrent profound episodes of hypoglycemia that may have been caused by tumor production of insulin-like growth factor. Cytology of urine has in most cases been unrewarding in identifying neoplastic cells, as has examination of abdominal fluid, although the latter had a hemorrhagic character in a small number of cases. Biopsy of the mass should be attempted to make a diagnosis.

Pyelonephritis and an intraabdominal abscess should be considered as primary differential diagnosis. With the exception of the nephroblastoma almost all reported cases are associated with significant metastasis to lung, liver,

and peritoneal cavity and/or local infiltration resulting in a poor prognosis. However some of these horses had prodromal signs for longer than 12 months and thus earlier intervention before metastasis could have made nephrectomy an option. Long-term (>17 months) treatment of right-sided renal adenocarcinoma has been successful by nephrectomy. Nephroblastomas should benefit from nephrectomy because they have not been associated with metastasis.

BLADDER

Primary equine bladder tumors are rare. The most commonly reported neoplasm of the bladder in older horses (ages 9-23 years) is the squamous cell carcinoma, followed by transitional cell carcinomas. Fibromatous polyp and lymphosarcoma are even rarer in this age group. A fibromatous polyp, rhabdomyosarcoma, and urachal cystadenoma were the only reported neoplasms in the bladder of horses younger than 3 years old. On the basis of these reports, mares seem to be twice as likely as male horses to develop primary bladder tumors.

Clinical Signs

The most common presenting complaint is stranguria, hematuria often with blood clots, and weight loss for less than several weeks' duration. Rectal palpation reveals a firm mass in the bladder that ultrasonographically seems to be part of the bladder wall. A bladder stone should be considered the most important differential diagnosis. Cystoscopy usually reveals irregular lobulated and ulcerated masses protruding into the bladder lumen. In cases in which the mass compromised the ureter outflow, a unilateral ureteral dilatation and pyelonephritis can be additional complications. Cytology of urine and that of fluid obtained by abdominocentesis is usually unproductive for detecting neoplastic cells. The most common laboratory abnormality is a low-grade anemia. A final diagnosis can be made from a biopsy sample. This can be obtained by endoscopy or perineal urethrostomy in males and via the urethra in mares. The prognosis for bladder neoplasms is poor.

Treatment

Surgical resection is difficult because of the accessibility and/or extent of bladder wall involvement. Additionally both squamous and transitional cell bladder carcinomas are locally invasive. Transitional cell carcinomas also have been reported to metastasize to the spleen, liver, and lung.

Therefore surgery may not be a realistic option. However, a urachal cystadenoma has been removed successfully from a racing filly.

Local instillation of 5-fluorouracil has been used to treat squamous cell carcinomas. Although this appeared to stop intraluminal growth, the horse was euthanized 2 weeks later because of ongoing local infiltrative growth of the tumor. Most horses with bladder neoplasms are euthanized within 3 months of diagnosis because of deterioration. However, at Michigan State University, a 17-year-old mare with a squamous cell carcinoma of the bladder survived 9 months as a result of monthly manual debulking of the tumor and 5-fluorouracil instillation (H.C. Schott, personal observation). The problem of surgical inaccessibility of the bladder potentially could be bypassed in mares by use of bladder eversion via the vagina in the standing horse. This technique is used successfully to repair bladder tears in adult mares.

EXTERNAL GENITALIA

The most frequently reported neoplasm of the equine external genitalia is a squamous cell carcinoma. The exact incidence of genital squamous cell carcinoma is not known but likely is lower than 1%, with a male-to-female ratio of 4:1. Geldings have been suggested to be more prone than stallions; however, this may be biased by the better hygienic care associated with breeding management of stallions and by the low number of intact males in the horse population. A breed predisposition for Appaloosas has been reported but the neoplasm has been reported in other breeds including ponies and draft horses. The sex and breed distribution, however, suggest that smegma (male, gelding) and UV-radiation on nonpigmented skin (Appaloosa) act as possible etiologic causes. The presence of a squamous papillomatous lesion on the equine penis may be a possible premalignant proliferation, especially because approximately 29% of penile squamous cell carcinomas are accompanied by squamous papillomas. Also gross examination has proven difficult in differentiation between squamous cell carcinoma and squamous papilloma.

Clinical Signs

The median age of diagnosis is between 12 and 19 years, although cases in animals as young as 4 years old have been reported. The most common presenting complaint for the male is a malodorous, often blood-stained, preputial discharge, or blood at the end of urination. In mares, growths were identified on the labia of the vulva. The real duration is often unknown because of inaccessibility of the penis, although the presence of a penile "growth" or discharge has been present for months up to 2 to 3 years in certain cases. In early stages, the neoplasm appears as a small, raised lesion or small ulcer, which progressed into a cauliflower-like or pedunculated mass with areas of necrosis, ulceration, and hemorrhage. Squamous cell carcinomas have a low grade of malignancy but eventually metastasize either hematogenously or via the lymphatic pathway resulting in intraabdominal and lung metastases.

Differential Diagnosis and Treatment

The differential diagnoses for genital squamous carcinoma should include squamous papilloma, sarcoid, melanoma, and habronemiasis. Differentiation can be made by biopsy. In the male genitalia, squamous cell carcinomas mostly involve the glans, body of the penis, and/or the internal preputial lamina. Smaller numbers are related to the external preputial lamina.

Treatment and prognosis depend on the size, and location of the neoplasm, the degree of infiltration, and the number of lesions. Local surgical debulking with or without local chemotherapy, local cryotherapy, or local radiation therapy has been successful for single noninfiltrating masses without evidence of metastasis. Topical application of 5-fluorouracil after debulking was successful in treating single noninfiltrating genital squamous cell carcinomas in a small number of geldings/stallions and mares. Prolonged presence of the drug in the sheath is believed to maintain local therapeutic levels, so on average, five treatments at 14-day intervals are needed. Daily topical application of 5-fluorouracil for up to 8 months after debulking is necessary to treat lesions in mares. Injections of cisplatin in a sesame oil base into the tumor at 2- to 3-week intervals have been successful in treating periocular squamous cell carcinomas in horses. Based on this result, genital treatment also seems promising. However, the tumor has a slowly infiltrating character and therefore extensive or multiple lesions should be treated with radical surgery such as partial phallectomy (penile resection) or *en bloc* resection of the penis, prepuce, and superficial lymph nodes with penile retroversion. Cases that involve the external preputial laminae only can be treated with a segmental posthetomy (reefing). Long-term follow-up (over 12 months without recurrence) for cases treated surgically is between 59% and 81%. The higher survival rate is in cases treated by *en bloc* resections.

After penile amputation, the most common postoperative complications are several weeks of intermittent bleeding after urination and edema that obstructs the urethrostomy site. Close observation and regular rectal examination is recommended to identify the latter problem. In such cases an indwelling catheter should be inserted for several days. Almost all tumor recurrence after surgery is in cases that already had thickening within the body of the penis by neoplasm with extension into the urethra, lymphatics, and vascular channels. The 18-month survival rate after phallectomy for these kind of cases is around 29%. Horses with rectally detectable enlarged inguinal lymph nodes die within 2 months because of generalized metastasis.

Client education on the necessity for good penile hygiene and regular inspection of the penis reduces the likelihood of tumor development and improves early detection and the outcome of penile squamous cell carcinoma treatment. Topical sunscreen also could be applied to the nonpigmented penile skin.

Supplemental Readings

Brown PJ, Holt PE: Primary renal cell carcinoma in four horses. *Equine Vet J* 1985; 17(5):473-477.

- Fischer AT, Spier S, Carlson GP et al: Neoplasia of the equine urinary bladder as cause of hematuria. *J Am Vet Med Assoc* 1985; 186:1294-1296.
- Fortier LA, Mac Harg MA: Topical use of 5-fluorouracil for treatment of squamous cell carcinoma of external genitalia of horses: 11 cases (1988-1992). *J Am Vet Med Assoc* 1994; 205:1183-1185.
- Gandini G, Pietra M, Cinotti S et al: Squamous cell carcinoma of the urinary bladder in a mare. *Equine Pract* 1998; 20:18-20.
- Gibson KT, Cantley C, Donald JJ et al: Urachal cystadenoma in a filly. *Aust Vet J* 1999; 77:638-640.
- Howarth S, Lucke VM, Pearson H: Squamous cell carcinoma of the equine external genitalia: a review and assessment of penile amputation and urethrostomy as a surgical treatment. *Equine Vet J* 1991; 23:55-58.
- Mair TS, Walmsley JP, Philips TJ: Surgical treatment of 45 horses affected by squamous cell carcinoma of the penis and prepuce. *Equine Vet J* 2000; 32:406-410.
- Rodgers DH, Spirito MA, Thorpe PE et al: Standing surgical repair of cystorrhhexis in two mares. *Vet Surg* 1999; 28:113-116.
- Sundberg JP, Burnstein T, Page ERH et al: Neoplasms of equidae. *J Am Vet Med Assoc* 1977; 170:150-152.
- Theon AP, Pascoe JR, Madigan JE et al: Comparison of intratumoral administration of cisplatin versus bleomycin for treatment of periocular squamous cell carcinomas in horses. *Am J Vet Res* 1997; 58:421-436.
- Traub-Dargatz JL: Urinary tract neoplasia. *Vet Clin North Am Equine Pract* 1998; 14:495-504.

CHAPTER 17.7

Urinary Tract Infection and Bladder Displacement

HAROLD C. SCHOTT II
East Lansing, Michigan

URETHRITIS, CYSTITIS, AND PYELONEPHRITIS

Bacterial infections of the urinary tract appear to be uncommon in horses. As in other species, ascending urinary tract infections (UTIs) are most common, although septic nephritis may be an occasional consequence of septicemia, especially in neonatal foals. Because of their shorter urethras, mares are at greater risk for UTIs than geldings or stallions, especially when they are used as breeding animals.

Urethritis

Bacterial urethritis has been described as a cause of hematuria, hemospermia, and/or stranguria in geldings and stallions. However, with the exception of traumatic, parasitic, or neoplastic conditions involving the distal urethra, this author is unaware of documented cases of primary bacterial urethritis. Bacterial infections of accessory sex glands or the prepuce may also cause dysuria. Preputial infections can occur as a consequence of trauma, neoplasia, habronemiasis, or presence of a foreign body. Owners present affected horses for a malodorous swollen sheath. Examination of the penis and sheath, in combination with biopsy of abnormal tissue, allows diagnosis of the primary problem. Occasionally an older gelding may develop recurrent sheath swelling and/or infection that cannot be attributed to a primary disease process. The pathogenesis of this problem is unknown, although fat accumulation, poor hygiene,

and inactivity may be contributing factors. Treatment involves repeated sheath cleaning, application of topical antiinflammatory and antibacterial ointments and, when more severe involvement occurs, systemic antibiotic administration.

Cystitis

Bacterial cystitis is usually a complication of urolithiasis, bladder neoplasia, bladder paralysis, or an anatomic defect of the bladder such as a persistent urachal remnant. Dysuria may be manifested by pollakiuria, stranguria, hematuria, and/or pyuria. Scalding and accumulation of urine crystals may be observed on the perineum of affected mares or on the front of the hindlimbs of affected male horses. These findings should not be confused with normal estrus activity in an occasional mare. Diagnostic evaluation includes physical and rectal examinations and collection of a urine sample for urinalysis and quantitative bacterial culture. Although the bladder is usually felt to be normal during rectal palpation, endoscopic examination of the bladder may be helpful in assessing mucosal damage caused by cystitis.

Because normal equine urine is rich in mucus and crystalloid material, gross examination may be unrewarding. However, sediment examination may reveal increased numbers of white blood cells (>10 leukocytes per high-power field) and presence of bacteria (>20 organisms per high-power field) in some, but not all, cases of cystitis.

- Fischer AT, Spier S, Carlson GP et al: Neoplasia of the equine urinary bladder as cause of hematuria. *J Am Vet Med Assoc* 1985; 186:1294-1296.
- Fortier LA, Mac Harg MA: Topical use of 5-fluorouracil for treatment of squamous cell carcinoma of external genitalia of horses: 11 cases (1988-1992). *J Am Vet Med Assoc* 1994; 205:1183-1185.
- Gandini G, Pietra M, Cinotti S et al: Squamous cell carcinoma of the urinary bladder in a mare. *Equine Pract* 1998; 20:18-20.
- Gibson KT, Cantley C, Donald JJ et al: Urachal cystadenoma in a filly. *Aust Vet J* 1999; 77:638-640.
- Howarth S, Lucke VM, Pearson H: Squamous cell carcinoma of the equine external genitalia: a review and assessment of penile amputation and urethrostomy as a surgical treatment. *Equine Vet J* 1991; 23:55-58.
- Mair TS, Walmsley JP, Philips TJ: Surgical treatment of 45 horses affected by squamous cell carcinoma of the penis and prepuce. *Equine Vet J* 2000; 32:406-410.
- Rodgers DH, Spirito MA, Thorpe PE et al: Standing surgical repair of cystorrhhexis in two mares. *Vet Surg* 1999; 28:113-116.
- Sundberg JP, Burnstein T, Page ERH et al: Neoplasms of equidae. *J Am Vet Med Assoc* 1977; 170:150-152.
- Theon AP, Pascoe JR, Madigan JE et al: Comparison of intratumoral administration of cisplatin versus bleomycin for treatment of periocular squamous cell carcinomas in horses. *Am J Vet Res* 1997; 58:421-436.
- Traub-Dargatz JL: Urinary tract neoplasia. *Vet Clin North Am Equine Pract* 1998; 14:495-504.

CHAPTER 17.7

Urinary Tract Infection and Bladder Displacement

HAROLD C. SCHOTT II
East Lansing, Michigan

URETHRITIS, CYSTITIS, AND PYELONEPHRITIS

Bacterial infections of the urinary tract appear to be uncommon in horses. As in other species, ascending urinary tract infections (UTIs) are most common, although septic nephritis may be an occasional consequence of septicemia, especially in neonatal foals. Because of their shorter urethras, mares are at greater risk for UTIs than geldings or stallions, especially when they are used as breeding animals.

Urethritis

Bacterial urethritis has been described as a cause of hematuria, hemospermia, and/or stranguria in geldings and stallions. However, with the exception of traumatic, parasitic, or neoplastic conditions involving the distal urethra, this author is unaware of documented cases of primary bacterial urethritis. Bacterial infections of accessory sex glands or the prepuce may also cause dysuria. Preputial infections can occur as a consequence of trauma, neoplasia, habronemiasis, or presence of a foreign body. Owners present affected horses for a malodorous swollen sheath. Examination of the penis and sheath, in combination with biopsy of abnormal tissue, allows diagnosis of the primary problem. Occasionally an older gelding may develop recurrent sheath swelling and/or infection that cannot be attributed to a primary disease process. The pathogenesis of this problem is unknown, although fat accumulation, poor hygiene,

and inactivity may be contributing factors. Treatment involves repeated sheath cleaning, application of topical antiinflammatory and antibacterial ointments and, when more severe involvement occurs, systemic antibiotic administration.

Cystitis

Bacterial cystitis is usually a complication of urolithiasis, bladder neoplasia, bladder paralysis, or an anatomic defect of the bladder such as a persistent urachal remnant. Dysuria may be manifested by pollakiuria, stranguria, hematuria, and/or pyuria. Scalding and accumulation of urine crystals may be observed on the perineum of affected mares or on the front of the hindlimbs of affected male horses. These findings should not be confused with normal estrus activity in an occasional mare. Diagnostic evaluation includes physical and rectal examinations and collection of a urine sample for urinalysis and quantitative bacterial culture. Although the bladder is usually felt to be normal during rectal palpation, endoscopic examination of the bladder may be helpful in assessing mucosal damage caused by cystitis.

Because normal equine urine is rich in mucus and crystalloid material, gross examination may be unrewarding. However, sediment examination may reveal increased numbers of white blood cells (>10 leukocytes per high-power field) and presence of bacteria (>20 organisms per high-power field) in some, but not all, cases of cystitis.

Quantitative culture results exceeding 10,000 organisms/ml in a urine sample collected by midstream catch or urethral catheterization are diagnostic for bacterial cystitis. For best results, urine sediment should be evaluated within 30 minutes of collection and samples for culture should be cooled during transport, because bacterial numbers may increase in samples left at room temperature. Organisms that may be recovered on culture include *Escherichia coli* and species of *Proteus*, *Klebsiella*, *Enterobacter*, *Corynebacterium*, *Streptococcus*, *Staphylococcus*, and *Pseudomonas*. Isolation of more than one organism is not uncommon.

Treatment

Successful treatment of bacterial cystitis requires correction of predisposing problems such as urolithiasis and administration of systemic antibiotics. Selection of an antibiotic is ideally based on the results of sensitivity testing of isolated organisms, and the initial course of treatment should not be less than 1 week. A trimethoprim/sulfonamide combination, ampicillin, penicillin and an aminoglycoside, or ceftiofur are initial alternatives. If clinical signs return after treatment is discontinued, a urine culture should be repeated and longer-term treatment instituted. In such cases, ease of administration and cost are additional considerations for antibiotic selection. For example, trimethoprim/sulfonamide combinations and the penicillins are excreted through the kidneys and concentrated in urine. Although sensitivity testing may indicate resistance, these agents may have effective antimicrobial activity against the causative agents because of the high concentrations achieved in urine.

Metabolism of the antibiotic should also be considered. As an example, sulfamethoxazole is largely metabolized to inactive products prior to urinary excretion, whereas sulfadiazine is excreted largely unchanged in urine. Next, addition of 50 g to 75 g salt to the diet or provision of warm water during cold weather may increase water intake and urine production, which are of benefit in cases of bacterial cystitis. Urinary acidifying agents including ammonium chloride (20 mg/kg per day PO) and vitamin C (2 g/kg per day PO) have also been administered to horses, but use of these agents at these doses has not produced a consistent decrease in urine pH. Use of ammonium chloride at a dose of 520 mg/kg per day by mouth or ammonium sulfate at 175 mg/kg per day by mouth was successful in reducing urine pH to below 6.0 in a limited number of horses. At these doses, the medications were unpalatable and had to be administered by dose syringe. Addition of grain to the diet is another simple way to decrease urine pH, although the decline is modest and urine pH typically remains higher than 7.0.

Upper Urinary Tract Infections

Upper urinary tract infections involving the kidneys and ureters are rare in horses. The course of the distal segment of the ureters in the dorsal bladder wall creates a physical barrier to vesiculoureteral reflux, which is a prerequisite for ascending pyelonephritis. Problems that interfere with this barrier and increase the risk for upper UTI include ectopic ureter or bladder distention as may occur with pregnancy, bladder paralysis, or urethral obstruction. Because

the kidneys are highly vascular organs, septic nephritis may develop in association with septicemia in neonatal or adult horses. Unless renal involvement is extensive, the upper UTI may go undetected but could lead to development of nephrolithiasis or chronic renal failure months or years later.

Horses with upper UTIs are more likely to have systemic clinical signs as presenting complaints, including fever, weight loss, anorexia, and depression. Upper UTI is often accompanied by stone formation that may lead to nephrolithiasis, ureterolithiasis, and signs of obstruction. Small uroliths may occasionally travel down the ureter and lead to urethral obstruction and renal colic as the presenting complaint. As for cystitis, diagnostic evaluation includes urinalysis, physical and rectal examinations, and a quantitative urine culture. In addition to the organisms listed earlier, organisms such as *Actinobacillus equuli*, *Streptococcus equi*, *Rhodococcus equi*, or *Salmonella* spp. can also be isolated from cases of hematogenous septic nephritis. In horses with upper UTIs, a complete blood count and serum biochemistry profile should be performed to assess the systemic inflammatory response and renal function. Cystoscopy, including watching for urine flow from each ureteral opening, and ultrasonographic imaging of the bladder, ureters, and kidneys are helpful adjunctive diagnostic procedures. Ureteral catheterization by passing polyethylene tubing through the biopsy channel of the endoscope or by use of an 8- to 10-French polypropylene catheter, which can be passed blindly in mares, may allow collection of urine samples from each ureter to distinguish unilateral from bilateral disease.

Treatment

Treatment for upper UTIs includes a prolonged course of appropriate systemic antibiotics and, in select cases with unilateral disease, surgical removal of the affected kidney and ureter. Although treatment successes are rare, poor outcomes are likely to be related to failure to diagnose an upper UTI until relatively late in the disease course.

BLADDER DISPLACEMENT

Displacement of the urinary bladder is a rare cause of obstruction and dysuria. In the mare, bladder displacements include extrusion through a tear in the vaginal floor or a true prolapse with bladder eversion. Urethral obstruction may also occur with vaginal or uterine prolapse. In the male horse, scrotal herniation of the bladder has been described, but this type of bladder displacement is extremely rare.

Bladder displacements are typically a consequence of repeated abdominal contractions and/or straining. Thus these displacements are most commonly associated with parturition and, to a lesser extent, with colic. Perineal lacerations consequent to trauma or foaling may lead to extrusion, whereas excessive straining without laceration leads to prolapse or eversion. Because the bladder turns inside out with the latter problem, the diagnosis is established by recognition of the appearance of the bladder mucosa and ureteral openings. Eversion does not always result in obstruction.

In cases of urethral obstruction, a catheter should be

passed into the bladder before correction of the displacement. In the absence of obstruction, extrusions are corrected during repair of the perineal or vaginal laceration. A course of broad-spectrum antibiotics and an antiinflammatory agent should be instituted because pelvic abscess and peritonitis are potential complications. In horses with bladder prolapse, application of hypertonic dextrose or saline solutions to the everted mucosa may decrease edema before manual replacement. Urethral sphincterotomy may be needed to replace the bladder and, in some cases, reduction through laparotomy may be necessary because the filling of the everted bladder by the colon complicates manual reduction.

Supplemental Readings

- Boyd WL, Bishop LM: Pyelonephritis of cattle and horses. *J Am Vet Med Assoc* 1937; 90:154-162.
- Divers TJ: Urinary tract infections. In Smith BP (ed): *Large Animal Internal Medicine*, 3rd edition, pp 834-836, St Louis, Mosby, 2002.
- Nouws JFM, Firth EC, Vree TB et al: Pharmacokinetics and renal clearance of sulfamethazine, sulfamerazine, and sulfadiazine and their N_4 -acetyl and hydroxy metabolites in horses. *Am J Vet Res* 1987; 48:392-402.
- Vaughn JT: Equine urogenital system. In Jennings PB (ed): *The Practice of Large Animal Surgery*, 2nd edition, pp 1136-1137, Philadelphia, WB Saunders, 1984.

CHAPTER 17.8

Acute Renal Failure

RAYMOND J. GEOR
Guelph, Ontario, Canada

Acute renal failure (ARF) is usually defined as an abrupt and sustained decrease in glomerular filtration rate with resultant azotemia and disturbances to fluid, electrolyte, and acid-base homeostasis. Acute renal failure may occur as a result of decreased renal perfusion (prerenal failure), primary renal dysfunction (intrinsic failure), or obstruction of urine flow (postrenal failure). In horses ARF is usually prerenal or renal in origin and is most often the result of hemodynamic or nephrotoxic insults. With the exception of bladder rupture in the neonate, postrenal failure is rare in the equine species.

The true prevalence of ARF in horses is unknown. However, it has been estimated that 0.5% to 1.0% of hospitalized horses have evidence of renal dysfunction. Horses at greatest risk for ARF include those with acute illness that results in hypovolemia and/or endotoxemia (e.g., colic, colitis, sepsis, and exhaustive exercise in warm conditions) and those with a history of treatment with potentially nephrotoxic drugs, particularly the aminoglycoside antibiotics, oxytetracycline, and the nonsteroidal antiinflammatory drugs (NSAIDs). Renal dysfunction is frequently reversible in the early stages of failure and prompt initiation of therapy often results in a favorable outcome. Conversely, treatment of established ARF often requires extensive supportive care and carries a guarded prognosis. Therefore it is imperative that renal function be routinely assessed in horses at high risk for development of ARF.

ETIOPATHOGENESIS

ARF in horses most commonly occurs secondary to conditions that result in alterations in systemic and renal hemodynamics or as a result of nephrotoxic insults (Box

17.8-1). The profound hypovolemia associated with acute gastrointestinal crises (proximal enteritis, colitis, strangulating intestinal obstructions), heavy exercise-associated sweat fluid losses, or blood loss can result in decreased cardiac output, hypotension, and renal hypoperfusion. Endotoxemia and sepsis may similarly impair renal blood flow (RBF). Initially the decrements in RBF and glomerular filtration rate (GFR) may not be associated with intrinsic renal dysfunction (prerenal failure). However, severe and/or prolonged renal hypoperfusion can result in ischemic injury to the renal tubules and interstitium, with resultant development of intrinsic renal failure.

Important nephrotoxins include the aminoglycoside antibiotics, oxytetracycline, and NSAIDs, particularly phenylbutazone. Acute tubular necrosis (ATN) may also develop consequent to exposure to endogenous pigments (myoglobin or hemoglobin), heavy metals (mercury-containing counterirritants), or vitamin D or K_3 (see Box 17.8-1). Acute glomerulonephritis that can occur after *Streptococcus equi* infection, interstitial nephritis associated with sepsis (*Actinobacillus equuli* in neonates or *Leptospira* spp. infection), or renal microvascular thrombosis (hemolytic uremic-like syndrome) are other less common causes of intrinsic renal failure.

Although the incidence of drug-induced nephrotoxicity is unknown, clinical experience suggests that the risk of renal dysfunction is greatest with the use of aminoglycoside antibiotics (see Chapter 17.11: "Once-Daily Aminoglycoside Dosing Regimens"), NSAIDs, and oxytetracycline, especially when these drugs are used in combination. Human patients with preexisting renal insufficiency and concurrent illness, particularly conditions that predispose to altered renal hemodynamics, are at greatest risk for

passed into the bladder before correction of the displacement. In the absence of obstruction, extrusions are corrected during repair of the perineal or vaginal laceration. A course of broad-spectrum antibiotics and an antiinflammatory agent should be instituted because pelvic abscess and peritonitis are potential complications. In horses with bladder prolapse, application of hypertonic dextrose or saline solutions to the everted mucosa may decrease edema before manual replacement. Urethral sphincterotomy may be needed to replace the bladder and, in some cases, reduction through laparotomy may be necessary because the filling of the everted bladder by the colon complicates manual reduction.

Supplemental Readings

- Boyd WL, Bishop LM: Pyelonephritis of cattle and horses. *J Am Vet Med Assoc* 1937; 90:154-162.
- Divers TJ: Urinary tract infections. In Smith BP (ed): *Large Animal Internal Medicine*, 3rd edition, pp 834-836, St Louis, Mosby, 2002.
- Nouws JFM, Firth EC, Vree TB et al: Pharmacokinetics and renal clearance of sulfamethazine, sulfamerazine, and sulfadiazine and their N_4 -acetyl and hydroxy metabolites in horses. *Am J Vet Res* 1987; 48:392-402.
- Vaughn JT: Equine urogenital system. In Jennings PB (ed): *The Practice of Large Animal Surgery*, 2nd edition, pp 1136-1137, Philadelphia, WB Saunders, 1984.

CHAPTER 17.8

Acute Renal Failure

RAYMOND J. GEOR
Guelph, Ontario, Canada

Acute renal failure (ARF) is usually defined as an abrupt and sustained decrease in glomerular filtration rate with resultant azotemia and disturbances to fluid, electrolyte, and acid-base homeostasis. Acute renal failure may occur as a result of decreased renal perfusion (prerenal failure), primary renal dysfunction (intrinsic failure), or obstruction of urine flow (postrenal failure). In horses ARF is usually prerenal or renal in origin and is most often the result of hemodynamic or nephrotoxic insults. With the exception of bladder rupture in the neonate, postrenal failure is rare in the equine species.

The true prevalence of ARF in horses is unknown. However, it has been estimated that 0.5% to 1.0% of hospitalized horses have evidence of renal dysfunction. Horses at greatest risk for ARF include those with acute illness that results in hypovolemia and/or endotoxemia (e.g., colic, colitis, sepsis, and exhaustive exercise in warm conditions) and those with a history of treatment with potentially nephrotoxic drugs, particularly the aminoglycoside antibiotics, oxytetracycline, and the nonsteroidal antiinflammatory drugs (NSAIDs). Renal dysfunction is frequently reversible in the early stages of failure and prompt initiation of therapy often results in a favorable outcome. Conversely, treatment of established ARF often requires extensive supportive care and carries a guarded prognosis. Therefore it is imperative that renal function be routinely assessed in horses at high risk for development of ARF.

ETIOPATHOGENESIS

ARF in horses most commonly occurs secondary to conditions that result in alterations in systemic and renal hemodynamics or as a result of nephrotoxic insults (Box

17.8-1). The profound hypovolemia associated with acute gastrointestinal crises (proximal enteritis, colitis, strangulating intestinal obstructions), heavy exercise-associated sweat fluid losses, or blood loss can result in decreased cardiac output, hypotension, and renal hypoperfusion. Endotoxemia and sepsis may similarly impair renal blood flow (RBF). Initially the decrements in RBF and glomerular filtration rate (GFR) may not be associated with intrinsic renal dysfunction (prerenal failure). However, severe and/or prolonged renal hypoperfusion can result in ischemic injury to the renal tubules and interstitium, with resultant development of intrinsic renal failure.

Important nephrotoxins include the aminoglycoside antibiotics, oxytetracycline, and NSAIDs, particularly phenylbutazone. Acute tubular necrosis (ATN) may also develop consequent to exposure to endogenous pigments (myoglobin or hemoglobin), heavy metals (mercury-containing counterirritants), or vitamin D or K_3 (see Box 17.8-1). Acute glomerulonephritis that can occur after *Streptococcus equi* infection, interstitial nephritis associated with sepsis (*Actinobacillus equuli* in neonates or *Leptospira* spp. infection), or renal microvascular thrombosis (hemolytic uremic-like syndrome) are other less common causes of intrinsic renal failure.

Although the incidence of drug-induced nephrotoxicity is unknown, clinical experience suggests that the risk of renal dysfunction is greatest with the use of aminoglycoside antibiotics (see Chapter 17.11: "Once-Daily Aminoglycoside Dosing Regimens"), NSAIDs, and oxytetracycline, especially when these drugs are used in combination. Human patients with preexisting renal insufficiency and concurrent illness, particularly conditions that predispose to altered renal hemodynamics, are at greatest risk for

BOX 17.8-1**Causes of Acute Renal Failure in Horses****Prerenal Failure**

Functional decrease in glomerular filtration rate associated with renal hypoperfusion

Hypotension and/or hypovolemia associated with the following:

1. Gastrointestinal fluid losses (colic, enterocolitis)
2. Acute blood loss
3. Exercise-associated sweat losses
4. Sepsis/endotoxemia
5. Volume redistribution (severe hypoalbuminemia; pleural or peritoneal effusion)
6. Disseminated intravascular coagulation

Intrinsic Renal Failure

Acute tubular necrosis secondary to the following:

- Profound and/or persistent renal hypoperfusion leading to ischemic necrosis (continuum from prerenal failure), especially in horses receiving nephrotoxic agents in the face of inadequate fluid replacement.
- Nephrotoxins
 1. Antimicrobial agents (aminoglycosides, tetracyclines)
 2. Heavy metals (mercury, arsenic, gold, lead)
 3. Endogenous substances (myoglobin, hemoglobin)
 4. Miscellaneous (NSAIDs, vitamin D, vitamin K3-menadione sodium bisulfite, cantharidin, acorns)
- Interstitial nephritis or glomerulonephritis secondary to bacterial infections (*Leptospirosis pomona*, *Actinobacillus equuli* in neonates, sequelae to *Streptococcus equi* infection [uncommon])
- Nephrolithiasis/ureterolithiasis

Postrenal Failure

Urinary bladder rupture (uoperitoneum) in neonates (rarely in postpartum mares)

NSAIDs, Nonsteroidal antiinflammatory drugs.

aminoglycoside- or NSAID-induced renal toxicity. Similarly, acutely ill horses that are dehydrated, hypovolemic, endotoxemic, septic, or hypoxemic are probably at greatest risk for drug-induced renal injury (Box 17.8-2). This observation emphasizes the importance of a thorough evaluation of renal function, including measurement of blood urea nitrogen (BUN) and serum creatinine (Cr) concentrations, before initiation of treatment with potentially nephrotoxic agents.

It is important to recognize that drug-induced ARF can occur in horses without obvious systemic illness or preexisting renal dysfunction, particularly when higher than recommended doses are administered. For example, oxytetracycline-induced ARF has been diagnosed in young horses receiving this drug for management of flexural deformities. The high doses of oxytetracycline recommended for treatment of tendon contracture in foals and weanlings

BOX 17.8-2**Risk Factors for Drug-Induced Nephrotoxicity****Patient-Related Factors**

Current or preexisting renal disease
Dehydration and volume depletion
Sepsis
Endotoxemia
Hypokalemia
Metabolic acidosis
Hypoxemia
Age (premature neonates)
Low-calcium diet (aminoglycosides)

Drug-Related Factors

Inherent nephrotoxic potential (high risk with aminoglycosides, tetracyclines, NSAIDs)
Dose
Duration and frequency of administration

Drug Interactions

Combined or closely associated use of drugs with added or synergistic nephrotoxic potential (e.g., aminoglycosides, NSAIDs, tetracyclines, diuretics)

NSAIDs, Nonsteroidal antiinflammatory drugs.

(44-70 mg/kg, once or twice) have been reported to be safe when administered to animals with normal renal function. However, it is not uncommon for foals or weanlings to receive these high doses for several days; this practice may increase the risk for nephrotoxicity. Additional risk factors would include mild dehydration caused by decreased nursing vigor or concurrent administration of an NSAID for pain relief, a not uncommon practice in the management of severe flexural deformities. The risk for oxytetracycline-induced renal injury is likely to be lower when this drug is administered at the doses recommended for treatment of bacterial infections or Potomac horse fever (5-10 mg/kg q12h). Nonetheless, assessment of renal function before and during treatment with oxytetracycline is recommended, particularly when high doses are administered.

Myoglobinuria and hemoglobinuria have both been associated with development of ARF in the horse (pigment nephropathy). Myoglobinuric nephrosis can develop secondary to exertional rhabdomyolysis, heat stroke, or extensive crush injuries. Causes of intravascular hemolysis and hemoglobinuria include incompatible blood transfusion, immune-mediated hemolytic anemia, fulminant hepatic failure, and toxicosis from ingestion of onions (*Allium* spp.) or withered red maple leaves (*Acer rubrum*). Although mechanisms of pigment nephropathy are poorly understood, myoglobin and hemoglobin may decrease RBF and local oxygen tension with resultant ischemic injury. Tubular pigment casts may also contribute to ischemic injury. In other species, concurrent hypovolemia and metabolic acidosis appear to potentiate the development of tubular injury by enhancement of free radical formation and lipid peroxidation of cell membranes.

CLINICAL SIGNS

In the majority of horses with ARF, clinical signs are usually referable to the primary problem, such as acute colic or enterocolitis, rather than to renal dysfunction. In general, the clinical manifestations of ARF reflect the systemic effects of toxic substances usually excreted in the urine (uremia); urinary tract dysfunction; and derangements of fluid, electrolyte, and acid-base balance. The predominant clinical signs of uremia in horses are depression and anorexia. Signs of encephalopathy (e.g., ataxia and mental obtundation) may occur in horses with severe azotemia.

Although oliguria is considered to be the hallmark of ARF, urine production in horses with ARF is variable. Oliguria frequently occurs in the early stages of hemodynamically mediated ARF, but anuria is rare. Nonoliguric ARF or polyuric ARF may also occur with exposure to nephrotoxins, and polyuria is common during the recovery phase of ARF. The magnitude of azotemia tends to be lower in nonoliguric ARF than oliguric ARF, possibly indicating less severe injury in nonoliguric ARF. Similarly, nonoliguric ARF is associated with a more favorable prognosis compared with oliguric ARF. In the clinical situation, affected patients are initially treated with large volumes of intravenous (IV) fluids for the primary disease (enterocolitis or colic) and oliguria progresses to polyuria. When significant renal damage has been sustained, persistence of oliguric ARF is usually recognized as failure to produce a significant volume of urine in response to fluid therapy, along with minimal change in the degree of azotemia over the initial day of treatment. If these patients are not carefully monitored, fluid retention may lead to development of subcutaneous and pulmonary edema. Soft feces caused by fluid retention may also be observed in patients with oliguric ARF.

Other clinical signs can include pyrexia, mild colic, dehydration, tachycardia, and injected or hyperemic mucous membranes. Colic signs may be more severe in horses with nephrolithiasis/ureterolithiasis; in these horses, evidence of hematuria and cystolithiasis may be present. Laminitis, which is frequently severe and rapidly progressive, is another potential sequela. Transrectal palpation may indicate enlargement of the left kidney, however, this assessment is subjective and normal kidney size does not rule out ARF. Horses with oliguric renal failure can have perirenal edema that may be detected through palpation per rectum or ultrasonographic examination.

DIAGNOSTIC EVALUATION

Diagnosis of ARF in horses is made on the basis of history, clinical signs, and results of urinalysis and serum biochemical analyses. Increases in BUN and Cr concentrations are frequently the initial findings that suggest compromised renal function. If azotemia is identified in horses with conditions such as enterocolitis, severe colic, or acute blood loss, it is important to differentiate whether azotemia is predominantly attributable to prerenal failure or intrinsic renal damage. With prerenal failure, volume repletion will restore renal function and the magnitude of azotemia should decrease by 50% or more during the initial day of treatment.

In contrast, with toxic or hemodynamic ARF, fluid therapy usually does not lead to prompt resolution of azotemia

and, in some cases, serum Cr continues to increase for a day or two despite intensive fluid therapy and an increase in urine output. Assessment of urine specific gravity before initiation of fluid therapy is helpful in the differentiation of prerenal from renal failure. Because normally functioning kidneys would maximally conserve salt and water in response to a transient decrease in RBF, urine specific gravity is typically greater than 1.035 (and may reach 1.050–1.060) with prerenal failure, whereas urine produced by horses with intrinsic ARF is often dilute (specific gravity <1.020) as a result of compromised concentrating ability. Additional measures that can be used to differentiate prerenal failure from intrinsic ARF include fractional sodium clearance (see Chapter 17.1: “Examination of the Urinary System”) and the ratios of urine to serum Cr and urine to serum osmolality. Intrinsic ARF can be inferred if the fractional sodium clearance is greater than 1.0%, the ratio of urine Cr to serum Cr is less than 37 (normal >50), or if the ratio of urine osmolality to serum osmolality is less than 1.7 (normal >2.5).

One problem with these laboratory assessments is that they are affected by fluid therapy. Thus application is limited to use on urine samples collected before initiation of fluid therapy or the first urine sample voided after fluid therapy has been started. In the clinical situation, assessment of the response to fluid therapy is the most practical way to differentiate prerenal failure from intrinsic renal failure. Azotemia caused by prerenal failure should resolve quickly with replacement of fluid deficits and restoration of renal perfusion. Finally, although prerenal failure and intrinsic ARF are often described as two separate entities, the distinction between the two is probably less clear and it is likely that some renal damage occurs in horses with prerenal failure. However, because of the considerable renal reserve capacity, renal damage associated with most conditions that result in transient renal hypoperfusion rarely affects case progression or outcome.

The most common electrolyte abnormalities in horses with ARF, particularly those with polyuric renal failure, are mild hyponatremia and hypochloremia. Serum potassium concentrations are variable; horses with oliguric or anuric ARF may be hyperkalemic whereas those with polyuric ARF, particularly anorectic patients, may be normokalemic or hypokalemic. With postrenal failure, especially when complicated by uroperitoneum, hyponatremia and hypochloremia are usually more severe and hyperkalemia is commonly found. Hypocalcemia and hyperphosphatemia may be additional findings with ARF. Affected horses often have a degree of metabolic acidosis, especially when ARF is associated with primary problems such as enterocolitis or severe colic.

As described previously, measures of urinary concentrating ability (specific gravity or osmolality) are helpful to assess development of intrinsic renal failure. Other abnormal urinalysis results can be sensitive indicators of renal damage. Significant indicators include changes in urine sediment such as increased numbers of erythrocytes, leukocytes, or presence of casts. Microscopic hematuria, proteinuria, and glucosuria may be additional findings with glomerular or tubular damage. Enzymuria, specifically the ratio of urinary γ -glutamyl transferase (GGT) activity to urinary Cr (uCr) concentration (see Chapter 17.1), has

been touted to be a sensitive indicator of renal tubular damage. Because GGT is too large to be filtered by the normal glomerulus and is present in large amounts in the brush border of proximal tubular epithelial cells, a urinary $\text{GGT} \div (\text{uCr} \times 0.01)$ value greater than 25 has been considered to be indicative of renal tubular disease. Measurement of urinary GGT activity has been advocated for early detection of aminoglycoside-induced renal disease. However, this ratio may be falsely elevated in sick horses through a decrease in Cr excretion, consequent to a reduction of GFR. Further, although urinary GGT activity may increase with aminoglycoside therapy, this finding does not necessarily foreshadow impending renal failure and, consequently, does not provide useful information regarding the need to modify the dosing regimen of or discontinue use of aminoglycosides.

Renal ultrasonography with a 3- or 5-MHz sector probe can provide useful information regarding renal size and structure. Other abnormalities such as perirenal edema, cystic cavities, or calculi (renal or ureteral) may be demonstrated by ultrasonographic examination. Percutaneous biopsy of the kidneys is possible in the standing horse, but the technique is not without complications including perirenal hematoma formation, hematuria, and/or hemo-peritoneum, and is only indicated when a renal mass or other abnormality of renal structure is recognized on ultrasonographic examination. Ultrasonographic guidance and use of a spring-loaded biopsy instrument (Temno Soft Tissue Biopsy Needle, ProAct Limited, State College, Pa.) may lessen the risk of complications.

THERAPY

Fluid therapy for correction of fluid deficits and electrolyte/acid-base abnormalities and promotion of increased urine output (diuresis) is the cornerstone of therapy for ARF, regardless of cause. In horses with prerenal failure that are at high risk for development of intrinsic ARF, the goal is to prevent or interrupt the pathophysiologic events that lead to development of intrinsic renal damage. The primary disease process that results in prerenal failure must also be identified and appropriately treated.

Ideally, administration of nephrotoxic drugs should be discontinued. However, in situations where continued administration of aminoglycoside antibiotics or NSAIDs is necessary, alterations in dosing regimens may lessen the risk of renal injury. With regard to the aminoglycosides, monitoring serum drug concentrations allows the clinician to individualize dosage regimens. For example, the risk of nephrotoxicity with aminoglycosides increases when trough concentrations remain high ($>2 \mu\text{g/ml}$ for gentamicin or $>5 \mu\text{g/ml}$ for amikacin). Serum trough concentrations can be reduced below these values by increasing the dosage interval (see Chapter 17.11: "Once-Daily Aminoglycoside Dosing Regimens"). When therapy with NSAID drugs is continued, the minimally effective dose should be used. Combinations of potentially nephrotoxic drugs (e.g., an aminoglycoside and an NSAID) should be avoided.

Blood samples for biochemical and acid-base analyses should be submitted before initiation of therapy. In addition,

packed cell volume, plasma total solids, and body weight should be determined. Although frequently overlooked, daily recording of body weight is perhaps the best measure of fluid balance in horses with fluid losses and renal dysfunction. Measurement of body weight is also critical to the correct determination of drug dosages. Deficit fluid requirements should be replaced during the first 6 to 12 hours of treatment. Physiologic saline (0.9% NaCl solution) is the fluid of choice unless hypernatremia is present, in which case a 0.45% NaCl/2.5% dextrose solution should be used. The clinician can calculate the amount of fluid required by multiplying the estimated dehydration (%) by body weight (kg). For example, for a 500-kg horse that is 8% dehydrated, the calculations are as follows:

$$0.08 \times 500 \text{ kg} = 40 \text{ kg} = 40 \text{ L}$$

In horses with prerenal failure, RBF, GFR, and urine output should return to normal after correction of the fluid deficit. Although the majority of horses with some degree of intrinsic ARF will increase urine production in response to fluid therapy, a few patients may remain oliguric after correction of fluid deficits. These horses must be closely monitored for signs of overhydration. Ideally, central venous pressure (normal values are $<8 \text{ cm H}_2\text{O}$) would be monitored in patients with oliguric ARF. However, daily measurement of body weight, packed cell volume, and plasma total solids; observation of respiratory rate and effort and auscultation of the lungs for sounds consistent with pulmonary edema; and observation for the development of dependent edema are more practical means to assess hydration state. Pulmonary edema can develop rapidly in horses with severe oliguric ARF; clinical experience has shown that as little as 40 ml/kg of IV fluids (20 L for a 500-kg horse) may result in pulmonary edema.

With the exception of horses with severe oliguric ARF or postrenal failure, serum potassium concentration is usually within normal limits and specific therapy intended to lower serum potassium concentration is not required. However, in select cases, recognition and treatment of hyperkalemia is essential as increases in serum potassium concentrations (to 6.5-7.0 mEq/L or higher) have the potential to induce cardiac arrhythmias including bradycardia, atrial standstill, and ventricular tachycardia. Moderate hyperkalemia usually resolves in response to administration of potassium-free fluids and improved urine flow. Horses with severe hyperkalemia ($>7.0 \text{ mEq/L}$) and cardiac arrhythmias should be treated with agents that decrease serum potassium concentration (sodium bicarbonate, 1-2 mEq/kg IV during 5 to 15 minutes) or counteract the effects of hyperkalemia on cardiac conduction. The latter can be accomplished by administration of calcium gluconate, 0.5 ml/kg of a 10% solution by slow IV injection or added to 5 L of IV fluids and administered during 1 hour.

Studies on myoglobin-induced nephropathy in animal models have demonstrated increased urinary myoglobin solubility and decreased tubular damage with alkalization of the urine. Therefore repeated administrations of sodium bicarbonate for urine alkalization may be indicated in horses with severe rhabdomyolysis and myoglobinuria.

Drug Treatments to Increase Renal Blood Flow and Urine Production

Furosemide (1.0-2.0 mg/kg IV every 6 hours), dopamine (3-5 μ g/kg/min IV in a 5% dextrose solution), or mannitol (0.25-1.0 g/kg as a 20% solution given IV during 15 to 20 minutes) have been advocated for treatment of oliguric ARF refractory to volume replacement therapy. The goal of these treatments is to increase RBF and urine production by renal vasodilation, diuresis, or a combination of these mechanisms. However, it must be emphasized that the efficacy of these treatments has not been assessed and, particularly for mannitol and dopamine, the risk of adverse effects with these agents may outweigh any theoretic benefit.

Of these agents, the loop diuretic furosemide is the most commonly used in an attempt to convert oliguric to nonoliguric ARF. Clinical experience, however, indicates wide variability in the urine output of horses with oliguric ARF following administration of the drug. The effect of furosemide on urine flow is dependent on intact GFR and tubular secretion for delivery of the drug to the active site in the tubular lumen. Tubular obstruction with cellular debris and pigments also can decrease tubular flow, thus limiting the delivery of furosemide to the active site. Taken together, these mechanisms may contribute to the variable, and often poor, diuretic response in horses with oliguric ARF. It is noteworthy that in human patients with ARF, furosemide treatment does not affect long-term outcome, although in some cases this therapy appears useful in the conversion of oliguric into nonoliguric renal failure. As furosemide administration has been demonstrated to exacerbate gentamicin toxicity in other species, its use is probably ill advised in horses with ARF secondary to aminoglycoside usage.

These limitations notwithstanding, judicious use of furosemide is recommended in horses with oliguric ARF. An initial dose of 1 to 2 mg/kg IV should be administered. If an increase in urine output is not observed after 45-60 minutes, a larger dose (4-6 mg/kg IV) should be administered. Large doses of furosemide may overcome the limitations in tubular drug delivery associated with the administration of more standard IV doses. If an increase in urine production is observed, furosemide administration should be continued at 1 to 3 mg/kg IV two to three times daily until clinical improvement is observed (e.g., partial resolution of azotemia). Obviously, IV fluid therapy must be continued during the period of furosemide treatment to avoid exacerbation of hypovolemia and renal hypoperfusion and injury. Electrolyte and acid-base status should also be monitored at regular intervals during therapy.

Anecdotally, dopamine has been widely used in the management of horses with ARF. Reports also exist of the administration of dopamine infusions to dehydrated, hypovolemic endurance horses, even before institution of adequate IV fluid replacement. It has been suggested that this treatment may attenuate renal injury associated with hypoperfusion. Studies in healthy horses have demonstrated a dose-dependent increase in RBF with administration of dopamine. At low doses (1-3 μ g/kg/min), this response likely reflects the renal arteriolar vasodilation by stimulation of dopamine receptors (subtype DA-1) on intrarenal vessels. At moderate doses (3-5 μ g/kg/min), an in-

crease in RBF may be attributable to inotropy (through stimulation of β -adrenoreceptors), whereas at high doses (5-20 μ g/kg/min) the enhanced RBF may be caused by increased perfusion pressure (through stimulation of α_1 -adrenoreceptors). However, studies in other species have indicated that the effects of dopamine are unpredictable and even with intermediate doses (3-5 μ g/kg/min) systemic vasoconstriction (through stimulation of α_1 -adrenoreceptors) can occur that offsets any beneficial effect of dopamine on RBF. Furthermore transient cardiac arrhythmias have been observed in healthy horses administered dopamine at 5 μ g/kg/min for 60 minutes. For these reasons, it is recommended that dopamine infusion for the management of oliguric ARF only be performed in hospitalized horses. Similarly, dopamine infusion is not recommended for the field treatment of dehydrated, hypovolemic, performance horses. The possibility exists that the arrhythmogenic and peripheral vasoconstrictor effects of dopamine are exacerbated in hypovolemic animals, with a potential worsening of renal hypoperfusion.

Dopamine is best administered with an infusion pump through a dedicated IV line. Addition of 120 mg of dopamine to 1 L of 0.9% NaCl or 5% dextrose will result in a dopamine concentration of 120 μ g/ml. A 500-kg horse would require 12.5 ml of this solution per minute for a desired infusion rate of 3 μ g/kg/min. Heart rate and rhythm should be monitored regularly during infusion, preferably by use of an electrocardiogram monitor.

The administration of mannitol, an osmotic agent, increases plasma osmolality and induces fluid shifts that increase effective circulating volume, RBF, and GFR. In the kidney, the osmotic effects of mannitol also may enhance tubular flow and urine output. However, the osmotic diuresis induced by mannitol may increase renal tubular oxygen demand, thereby increasing susceptibility to ischemic injury. Indeed, in other species evidence exists that high doses of mannitol (3 g/kg) exacerbate ARF. For these reasons mannitol is no longer recommended in the management of oliguric ARF in human patients. It should also be noted that the use of an osmotic diuretic agent is contraindicated in overhydrated patients, because the associated increase in intravascular volume may precipitate pulmonary edema.

Adjunct Therapies and Clinical Monitoring

Once volume deficits have been corrected and diuresis has been established, fluid therapy should be tailored to provide for maintenance requirements. This author uses 55 to 60 ml/kg/day (or 1 L/hr to a 400- to 500-kg horse) as an estimate of daily fluid requirements for adult horses. However, during the polyuric recovery phase of ARF, urine volume and urinary electrolyte losses can be increased, and maintenance fluid requirements may be two to three times greater than those of healthy horses. Potassium supplementation (20-40 mEq of KCl added to each liter of IV fluids) may be necessary, particularly for anorectic patients. An estimate of the volume of ongoing fluid losses for the primary disease process (e.g., enterocolitis) should also be included in the daily plan for fluid administration. Polyionic fluids such as lactated Ringer's solution should be used once electrolyte and acid-base alterations have

been corrected. Oral electrolyte therapy (e.g., 30 g NaCl once or twice daily, administered as a slurry through dosing syringe) is also useful for encouragement of water consumption and urine output. In normokalemic, anorectic horses, the administration of potassium chloride (15-30 g PO twice daily) is also indicated.

Protracted ARF and anorexia can lead to a catabolic state, and affected patients often require nutritional support. Enteral feeding through a nasogastric tube (see Chapter 13.2: "Clinical Assessment of Nutritional Status and Enteral Feeding in the Acutely Ill Horse" and Chapter 13.4: "Nutritional Support in Selected Metabolic, Hepatic, Urinary, and Musculoskeletal Conditions") is the most economical method of nutritional support. Adding dextrose to IV fluids (5%-10% solution) may provide some nutritional support, but the calories provided will not meet minimum daily requirements. Critical illness and protracted inanition can also increase the risk of gastric ulceration. Therefore treatment with omeprazole (2-4 mg/kg PO q24h) or cimetidine (8-10 mg/kg IV q8h) is warranted.

Frequent patient monitoring is essential to assess response to therapy. The minimum data collected on a daily basis should include clinical assessment, body weight, packed cell volume, plasma total solids, serum concentrations of Cr and electrolytes, and volume of fluid administered. IV fluid therapy should be continued until the horse is eating and drinking normally and a substantial decrease (>75%) in Cr concentration has occurred. The volume of fluids administered should be reduced gradually during a 2- to 3-day period before discontinuing fluid therapy. It is important to monitor the patient's hydration status during this period. The serum Cr concentration should be measured again 2 to 3 days after fluid therapy is discontinued.

PROGNOSIS

The prognosis for ARF in the horse depends on the underlying cause, duration of renal failure, response to initial treatment, and development of secondary complications such as laminitis, thrombophlebitis, and diarrhea. Regardless of the cause, the duration of renal failure before initiation of therapy is the most important determinant of prognosis. Early interruption of the pathophysiologic events that lead to ARF provides the best chance of pre-

venting permanent renal dysfunction. Horses with hemodynamically-mediated ARF secondary to conditions such as diarrhea, endotoxemia, hemolytic crises, and myopathy usually have a good prognosis for full recovery of renal function provided that appropriate therapy is instituted and the primary problem can be corrected.

The expected response to therapy in patients with pre-renal failure (serum Cr typically <5 mg/dl) is rapid resolution of azotemia during the first 2 to 3 days of treatment. Patients with a favorable prognosis for recovery from intrinsic ARF (serum Cr may range from 5-10 mg/dl) have a more gradual decline in serum Cr concentration during a 3- to 7-day period, although complete resolution of azotemia may take 4 to 6 weeks. A more guarded prognosis should be given for patients with serum Cr greater than 10 mg/dl at initial evaluation and when azotemia is unchanged or worse after the first day or two of treatment. The prognosis is poor for horses with more severe azotemia at initial evaluation (Cr >15 mg/dl) and for those that remain oliguric 24 to 48 hours after the start of intensive treatment. In these horses, a high incidence of secondary complications such as generalized edema and laminitis contributes to the poor prognosis.

Supplemental Readings

- Bartol JM, Divers TJ, Perkins GA: Nephrotoxicant-induced acute renal failure in five horses. *Comp Cont Educ Pract Vet* 2000; 23:870-876.
- Dishart MK, Kellum JA: An evaluation of pharmacological strategies for the prevention and treatment of acute renal failure. *Drugs* 2000; 59:79-91.
- Divers TJ, Whitlock RH, Byars TD et al: Acute renal failure in six horses resulting from hemodynamic causes. *Equine Vet J* 1987; 19:178-184.
- Geor RJ: Drug-induced nephrotoxicity: recognition and prevention. *Comp Cont Educ Pract Vet* 2000; 23:876-878.
- Rossier Y, Divers TJ, Sweeney RW: Variations in urinary gamma glutamyl transferase/urinary creatinine ratio in horses with or without pleuropneumonia treated with gentamicin. *Equine Vet J* 1005; 27:217-220.
- Vivrette S, Cowgill LD, Pascoe J et al: Hemodialysis for treatment of oxytetracycline-induced acute renal failure in a neonatal foal. *J Am Vet Med Assoc* 1993; 203:105-107.

CHAPTER 17.9

Chronic Renal Failure

HAROLD C. SCHOTT II
East Lansing, Michigan

Chronic renal failure is a well-recognized but infrequently diagnosed syndrome in the horse. One widely cited abattoir study revealed that 16% of horses examined had glomerular lesions on light microscopy and 36% exhibited deposits of immunoglobulin and/or complement on immunofluorescent testing. Although these findings suggest that as many as one third of horses may have renal disease, only one of the horses in this survey exhibited signs of chronic renal failure. This disparity can be attributed to a large renal reserve capacity because clinical signs of chronic renal failure do not become apparent until two thirds to three fourths of functional nephrons have been lost.

ETIOLOGY

Disorders of the kidneys leading to chronic renal failure may be congenital or acquired. In patients younger than 5 years and lacking a history of an event that may have been complicated by acute renal failure, congenital renal disorders should be suspected. These disorders may include renal agenesis, dysplasia, hypoplasia, polycystic kidney disease, and hydronephrosis (see Chapter 17.3: "Congenital Disorders of the Urinary Tract"). Although each of these congenital abnormalities is occasionally recognized, acquired disorders are the more common cause of chronic renal failure in horses.

Acquired disease may be a consequence of tubular or glomerular damage. Tubulointerstitial disease usually occurs as a sequela to an episode of acute tubular necrosis. Renal ischemia and nephrotoxic compounds are the mechanisms of damage. Hypovolemia associated with colic, diarrhea, sepsis, or acute blood loss can lead to renal hypoperfusion and ischemic damage. Aminoglycoside antibiotics, nonsteroidal antiinflammatory drugs, vitamin D, vitamin K₃, and heavy metals such as mercury are all potentially nephrotoxic. Intravascular hemolysis or rhabdomyolysis can also lead to acute tubular damage consequent to the nephrotoxic effects of hemoglobin or myoglobin. In addition, severe tubulointerstitial disease culminating in chronic renal failure may develop consequent to ascending urinary tract infection, resulting in bilateral pyelonephritis or bilateral obstructive disease with ureteroliths or nephroliths (see Chapter 17.5: "Obstructive Disease of the Urinary Tract").

Immune-mediated glomerular injury is another initiating cause of chronic renal failure in horses. Glomerular injury is typically the result of deposition of circulating immune complexes along the glomerular basement membrane and in the mesangium. In rare cases glomerulone-

phritis may be attributed to a true autoimmune disorder in which antibodies directed against the glomerular basement membrane are produced. Both immune mechanisms lead to complement activation, leukotaxis, and lysosomal degranulation that damages the glomerular capillaries and leads to glomerulosclerosis. Thickening of the filtration barrier leads to a progressive decline in glomerular filtration rate and development of azotemia. Both streptococcal antigens and equine infectious anemia virus have been demonstrated to be associated with development of glomerulonephritis in horses. Renal amyloidosis is an unusual cause of glomerulopathy and is somewhat unique to horses that are hyperimmunized for serum production. Another acquired cause of chronic renal failure is renal neoplasia. Although rare in the horse, the most common primary renal neoplasm is renal cell carcinoma, which is usually a unilateral lesion that does not result in azotemia.

CLINICAL SIGNS

Chronic weight loss is the most common presenting complaint for horses with chronic renal failure. Lethargy, rough hair coat, partial anorexia, ventral edema, polyuria and polydipsia, and poor athletic performance also are frequent owner concerns. Deterioration of body condition and lethargy may be attributable to several factors. As the magnitude of azotemia increases, clinical signs of uremia develop. An increase in the concentration of nitrogenous wastes in blood can have a direct central appetite suppressant effect that may lead to partial or complete anorexia. In the later stages of uremia, urea may be converted to ammonia by oral bacteria and may lead to oral ulceration, uremic halitosis, and excessive dental tartar formation. Uremic gastroenteritis may further lead to mild-to-moderate ulcer disease and a protein-losing enteropathy. Severely affected animals may develop soft feces.

Alterations in the integrity of the highly anionic glomerular filtration barrier can also lead to loss of protein, predominantly albumin, in the urine. In some cases, protein loss may be great enough to lead to a decline in plasma protein concentration; however, horses appear to be more refractory to development of severe proteinuria, hypoproteinemia, and the nephrotic syndrome than small animal veterinary patients with chronic renal failure. In some cases with a normal total plasma protein concentration, an increase in globulin concentration offsets mild hypoalbuminemia, whereas in other cases hyperglobulinemia may result in an increase in total plasma protein concentration. A decrease in the albumin-to-globulin ratio

is found in these horses. Most importantly, the combined effects of uremia with or without severe proteinuria place the affected patient in a catabolic state in which body mass declines as body reserves are tapped to meet basal energy requirements.

Mild ventral edema is a common but inconsistent finding in horses with chronic renal failure and may be attributable to three factors—decreased oncotic pressure, increased vascular permeability, and increased hydrostatic pressure. An albumin concentration below 1.0 to 1.5 g/dl is usually required before plasma oncotic pressure is significantly reduced. Because this degree of hypoalbuminemia is rare in horses with chronic renal failure, uremic vasculitis causing increased vascular permeability may be a more important factor in the development of edema in patients without hypoalbuminemia. In addition, chronic renal insufficiency can lead to renal hypoxia and hypoperfusion, which are stimuli for renal juxtaglomerular cells to release renin. Activation of the renin-angiotensin system tends to elevate hydrostatic pressure and contributes to edema formation. Unlike small animal and human patients, alterations in blood pressure in horses with chronic renal failure have not been documented.

Polyuria and polydipsia are variable findings in horses with chronic renal failure. The degree of polyuria and polydipsia is theoretically related to the degree of tubulointerstitial damage; however, the degree of polyuria does not appear to be correlated with the magnitude of azotemia in clinical cases. Typically, polyuria with chronic renal failure is not as severe as with diabetes insipidus or psychogenic water drinking, and it may go unobserved by the owner. The wide variation in water intake in normal horses and common use of automatic waterers and large stock tanks further make polydipsia less apparent to owners.

An early complaint for horses with chronic renal failure may be decreased performance. Poor performance is most likely related to mild anemia, packed cell volume of 20% to 30%, and lethargy. In fact, administration of genetically engineered erythropoietin to human patients awaiting renal transplantation has been one of the most significant advances in management of chronic renal failure in people. This treatment has improved exercise capacity and decreased morbidity associated with the uremic syndrome. This observation suggests that mild exercise can have a positive impact during the early stages of chronic renal failure in horses.

DIAGNOSIS

A diagnosis of chronic renal failure is established when persistent isosthenuria accompanies azotemia and typical clinical signs. Results of rectal palpation of the left kidney may be normal or may suggest a smaller than normal kidney. In rare cases the kidneys and ureters may be enlarged if obstructed by uroliths or if infection or neoplasia is present. Common clinicopathologic findings accompanying chronic renal failure include a mild normocytic, normochromic anemia; variable hypoalbuminemia and hypoproteinemia; mild hyponatremia and hypochloremia; hypercalcemia and hypophosphatemia; and a low plasma bicarbonate concentration. As suggested earlier, a nonregenerative anemia is related in part to a deficient supply of

the renally secreted glycoprotein, erythropoietin. However, reduced erythrocyte lifespan may be a more significant factor contributing to anemia. Normally, the equine erythrocyte has a lifespan of 150 to 155 days. In the uremic patient, lifespan is shortened because excessive nitrogenous waste products alter protective mechanisms of the red cell membrane. These less resilient cells are more likely to be removed from the circulation by the reticuloendothelial system.

Electrolyte alterations are a consequence of the loss of tubular function. Because sodium, chloride, bicarbonate, and phosphate are conserved by renal tubules, chronic renal failure may be accompanied by excessive urinary loss of these electrolytes and a degree of metabolic acidosis unless hypochloremia becomes severe, allowing metabolic alkalosis to develop. Although fractional electrolyte clearance values (see Chapter 17.1: "Examination of the Urinary System") may remain within normal ranges or may increase only slightly in horses with chronic renal failure, significant daily urinary loss of electrolytes may still occur. As an example, consider a horse with chronic renal failure with serum creatinine and sodium concentrations of 5.0 mg/dl and 130 mEq/L, respectively. If the horse is producing 30 L of urine daily with respective creatinine and sodium concentrations of 50 mg/dl and 13 mEq/L, the fractional clearance of sodium is 1.0% with a daily urinary sodium loss of 390 mEq. An increase in urinary sodium concentration to 26 mEq/L resulting from a further decrease in tubular reabsorption would result in an increase in fractional sodium clearance to 2% but would represent an additional 390 mEq of daily sodium loss in the urine. The latter value represents approximately 3% of the exchangeable sodium content of the body; an additional 20 to 25 g of daily salt intake would be needed to accommodate this loss. This example illustrates the importance of providing adequate access to salt, in addition to water, to horses with chronic renal failure.

Hypercalcemia is a unique finding in horses with chronic renal failure, and the magnitude of hypercalcemia is dependent on the amount of calcium in the diet. Hypercalcemia is not the result of hyperparathyroidism, because parathormone concentrations in horses with chronic renal failure appear to be decreased. Because the equine kidney is an important route of calcium excretion (via calcium carbonate crystals), impaired tubular function in the face of continued intestinal absorption results in calcium accumulation in blood. This simplified explanation is supported by the similar development of hypercalcemia after experimental bilateral nephrectomy in ponies.

The influence of dietary calcium can be demonstrated by changing the type of hay fed to horses with chronic renal failure. In patients with serum calcium concentrations exceeding 20 mg/dl on a predominantly alfalfa diet, serum calcium concentrations can return to the normal range within a couple of days after the diet is changed to grass hay. It remains unknown whether the presence of hypercalcemia in horses with chronic renal failure is associated with exacerbation of the renal disease or tissue mineralization.

Urinalysis in horses with chronic renal failure typically reveals persistent isosthenuria with a urine specific gravity of 1.008 to 1.014. In an exceptional case with significant

proteinuria, this value may increase to 1.020 to 1.025. The amount of crystals and mucus is much reduced because of the dilute nature of the urine. In general, urine sediment is free of red cells, leukocytes, casts, and bacteria except in cases of pyelonephritis. Bacterial culture of an appropriately collected urine sample should be performed in all cases because pyelonephritis is not always accompanied by obvious urine sediment abnormalities.

Additional diagnostic tests include renal ultrasonography to evaluate kidney size and to look for cysts or nephroliths. Horses with chronic renal failure typically have slightly smaller kidneys that are more echogenic than normal because of sclerosis and possible tissue mineralization. Renal biopsy with ultrasonographic guidance may be performed to document the presence of renal disease. Unfortunately, because most horses are presented for evaluation in the later stages of disease, biopsy results typically reveal glomerular, tubular, and interstitial lesions consistent with end-stage kidney disease. Rarely do the lesions provide information about the inciting cause of the renal disease, unless immunofluorescent testing is pursued. The latter requires placing a sample in special media (contact testing laboratory for specific recommendations), in addition to a second sample placed in formalin for routine histopathology examination. In some cases, renal biopsy results supporting pyelonephritis or a congenital anomaly (dysplasia) as the cause of chronic renal failure help to develop a therapeutic plan.

Assessment of the severity of renal disease can be performed at many levels of sophistication. The magnitude of azotemia is the most readily available parameter, but it is a relatively insensitive and variable measure. Azotemia becomes apparent only after 75% or more of renal function has been lost. In addition, the degree of azotemia may vary with nonrenal factors such as diet, body mass, and hydration. In general, serum creatinine concentration is a more reliable measure than urea nitrogen concentration. Serum creatinine concentrations in the range of 10 to 12 mg/dl indicate a marked decline in renal function, and values exceeding 15 mg/dl are consistent with a grave prognosis. Although measurement of glomerular filtration rate is more time-consuming and technically demanding, it provides a more accurate quantitative assessment of renal function (see Chapter 17.1: "Examination of the Urinary System").

TREATMENT

Once significant renal disease becomes established, an irreversible decline in glomerular filtration rate and progression of renal failure generally ensue. Thus management of the equine patient afflicted with chronic renal failure involves palliative efforts to minimize further loss of renal function. The goals are management to prevent complicating conditions such as a lack of water or salt availability, to discontinue administration of nephrotoxic agents, and to provide a palatable diet to stimulate the appetite and minimize further weight loss. Intravenous (IV) fluid therapy to cause diuresis is of much greater benefit in cases with acute, reversible renal failure but may also be of benefit to the patient that suffers a sudden exacerbation of chronic renal failure. IV fluid therapy must be ad-

ministered cautiously to patients with chronic renal failure, because significant pulmonary edema may develop in patients with transient oliguria or anuria.

Supportive therapy may include supplementation of sodium chloride (25-50 g/day PO), possibly in combination with sodium bicarbonate (50-150 g/day PO) when serum bicarbonate concentration is consistently lower than 20 mEq/L. Supplemental electrolytes may need to be added to bran mashes or administered as pastes because horses may not ingest adequate amounts from licking a salt block. If electrolyte supplementation aggravates ventral edema, the amount should be decreased. Substitution of high-calcium and high-protein feed sources such as alfalfa hay with good-quality grass hay and carbohydrates such as corn and oats may help control hypercalcemia and the level of azotemia. Ideally, the hay and grain should contain less than 10% crude protein, which is an adequate but not excessive amount, and should maintain the blood urea nitrogen (BUN)-to-creatinine ratio within a target range of 10:1 to 15:1. Although advocated in the past, a lower-protein diet does not appear to be of benefit in slowing progression of renal failure. It is important to provide unlimited access to fresh water and to encourage adequate energy intake by the availability of a variety of palatable feeds. In fact, if appetite for grass hay deteriorates, it is preferable to offer less ideal feeds such as alfalfa hay or increased amounts of concentrate to meet energy requirements and lessen the degree of wasting. Administration of B vitamins or anabolic steroids for their touted appetite-stimulating effects may be of benefit in some animals. Although dietary fat supplementation may provide a dense source of calories, it must be approached judiciously because some uremic patients may develop hyperlipidemia as a result of reduced triglyceride use. In addition, hyperlipidemia is associated with progressive loss of renal function in dogs. Edema is usually not a significant problem, and, unless it interferes with ambulation, it should be tolerated rather than treated with diuretic agents that may be ineffective or may lead to further electrolyte wastage.

Specific treatment for chronic renal failure such as renal transplantation is not available for horses. An exception is with pyelonephritis (see Chapter 17.7: "Urinary Tract Infection and Bladder Displacement") in which specific antibiotic treatment is warranted. The progressive renal injury that occurs in chronic renal failure is associated with continued damage to tubular and glomerular membranes mediated by ongoing activation of the inflammatory cascade. Although not supported by experimental data in the horse, treatment with antioxidant medications and free radical scavengers could, in theory, be of benefit.

Interest has arisen in the role of dietary fatty acids as precursors of eicosanoids. Specifically dietary supplementation with sources rich in omega-3-fatty acids (linolenic acid)—as compared with omega-6-fatty acids (linoleic acid)—appears to decrease generation of more damaging fatty acid metabolites during activation of the inflammatory cascade. In horses, dietary supplementation with omega-3-fatty acids in the form of linseed oil has been effective at ameliorating the effects of endotoxin in *in vitro* studies. Supplementation with menhaden oil, another rich source of omega-3-fatty acids, slows the progression

of renal failure in dogs. Unfortunately, the *in vivo* effects of endotoxin were not ameliorated by feeding linseed oil in preliminary equine studies, and the possible benefits of feeding omega-3-fatty acids to horses with chronic renal failure are unknown at this time.

Although administration of corticosteroids or non-steroidal antiinflammatory drugs also limits the inflammatory response, their negative effects on renal blood flow outweigh the possible beneficial effects, and they are not recommended in the treatment of chronic renal failure in horses. Administration of synthetic prostaglandin-E analogues is another treatment that, in theory, could increase renal blood flow and ameliorate progression of chronic renal failure. However, no data are available to support use of these treatments at this time.

PROGNOSIS

Most horses diagnosed with chronic renal failure exhibit obvious weight loss and other clinical signs at the time of presentation. Because of the progressive and irreversible nature of the renal disease, the long-term prognosis is grave. However, the short-term prognosis for nonoliguric patients may be more favorable. Some horses with chronic renal failure may maintain serum creatinine concentrations between 3 and 6 mg/dl for months with minimal deterioration, whereas other horses with similar laboratory data may lose weight rapidly. Prediction of which cases will deteriorate more rapidly is difficult, but a recent history and initial ability to counteract weight loss with improved management are useful indicators. Laboratory analysis of blood samples at 2- to 4-week intervals to follow the degree of azotemia and serum electrolyte alterations may be useful in monitoring disease progression. Extrapolation of the decline of the reciprocal of serum cre-

atinine (1/Cr) over time has been used in some cases to estimate disease progression. However, this calculation assumes a constant rate of decline in remaining renal function and, when applied to many human patients and to a few equine patients this author has studied, the technique has been unrewarding because the course of disease is not constant or predictable.

In general, animals that are eating well and maintaining reasonable body condition carry the best short-term prognosis and may still be able to perform a limited amount of work. Their usefulness as breeding animals may be reduced because azotemia and cachexia can reduce the chance for normal conception and gestation. The goal in each case is to monitor the horse closely to be able to provide euthanasia before the patient reaches a state of uremic decompensation.

Supplemental Readings

- Divers TJ: Chronic renal failure in horses. *Comp Cont Educ Pract Vet* 1983; 5:S310-S317.
- Divers TJ: Management of chronic renal failure in the horse. *Proceedings of the 31st Annual Convention of the American Association of Equine Practitioners*, pp 679-681, 1985.
- Klahr S, Schreiner G, Ichikawa I: The progression of renal disease. *N Engl J Med* 1988; 318:1657-1666.
- Koterba AM, Coffman JR: Acute and chronic renal disease in the horse. *Comp Cont Educ Pract Vet* 1981; 3:S461-S469.
- Schott HC, Patterson KS, Fitzgerald SD et al: Chronic renal failure in 99 horses. *Proceedings of the 43rd Annual Convention of the American Association of Equine Practitioners*, pp 345-346, 1997.
- Tennant B, Kaneko JJ, Lowe JE et al: Chronic renal failure in the horse. *Proceedings of the 23rd Annual Convention of the American Association of Equine Practitioners*, pp 293-297, 1978.

CHAPTER 17.10

Renal Tubular Acidosis in Horses

MONICA ALEMAN
Davis, California

Renal tubular acidosis (RTA) is characterized by altered renal tubular function, resulting in a profound hyperchloremic metabolic acidosis with a normal anion gap. Renal tubular acidosis has been reported in humans, dogs, cats, and horses. In horses, RTA can be primary (idiopathic) or secondary to other concurrent disease. Although drug-induced RTA has not been reported in horses, some of the drugs implicated in the development of RTA in humans are used widely in horses. Such drugs are carbonic anhydrase inhibitors, potassium-sparing diuretics, β -adrenergic adrenoceptor

blockers, angiotensin-converting enzyme inhibitors, cyclosporin A, gentamicin, amphotericin B, trimethoprim/sulfamethoxazole, outdated tetracyclines, and non-steroidal antiinflammatory agents. Renal tubular acidosis should be considered as a differential diagnosis in horses that present with vague signs of depression, poor performance, anorexia, and weight loss. The key for its diagnosis is the finding of a profound hyperchloremic metabolic acidosis in a routine biochemical profile.

Horses can apparently have type I or II RTA or a combination of both. Type I RTA develops when the distal tubules

of renal failure in dogs. Unfortunately, the *in vivo* effects of endotoxin were not ameliorated by feeding linseed oil in preliminary equine studies, and the possible benefits of feeding omega-3-fatty acids to horses with chronic renal failure are unknown at this time.

Although administration of corticosteroids or non-steroidal antiinflammatory drugs also limits the inflammatory response, their negative effects on renal blood flow outweigh the possible beneficial effects, and they are not recommended in the treatment of chronic renal failure in horses. Administration of synthetic prostaglandin-E analogues is another treatment that, in theory, could increase renal blood flow and ameliorate progression of chronic renal failure. However, no data are available to support use of these treatments at this time.

PROGNOSIS

Most horses diagnosed with chronic renal failure exhibit obvious weight loss and other clinical signs at the time of presentation. Because of the progressive and irreversible nature of the renal disease, the long-term prognosis is grave. However, the short-term prognosis for nonoliguric patients may be more favorable. Some horses with chronic renal failure may maintain serum creatinine concentrations between 3 and 6 mg/dl for months with minimal deterioration, whereas other horses with similar laboratory data may lose weight rapidly. Prediction of which cases will deteriorate more rapidly is difficult, but a recent history and initial ability to counteract weight loss with improved management are useful indicators. Laboratory analysis of blood samples at 2- to 4-week intervals to follow the degree of azotemia and serum electrolyte alterations may be useful in monitoring disease progression. Extrapolation of the decline of the reciprocal of serum cre-

atinine (1/Cr) over time has been used in some cases to estimate disease progression. However, this calculation assumes a constant rate of decline in remaining renal function and, when applied to many human patients and to a few equine patients this author has studied, the technique has been unrewarding because the course of disease is not constant or predictable.

In general, animals that are eating well and maintaining reasonable body condition carry the best short-term prognosis and may still be able to perform a limited amount of work. Their usefulness as breeding animals may be reduced because azotemia and cachexia can reduce the chance for normal conception and gestation. The goal in each case is to monitor the horse closely to be able to provide euthanasia before the patient reaches a state of uremic decompensation.

Supplemental Readings

- Divers TJ: Chronic renal failure in horses. *Comp Cont Educ Pract Vet* 1983; 5:S310-S317.
- Divers TJ: Management of chronic renal failure in the horse. *Proceedings of the 31st Annual Convention of the American Association of Equine Practitioners*, pp 679-681, 1985.
- Klahr S, Schreiner G, Ichikawa I: The progression of renal disease. *N Engl J Med* 1988; 318:1657-1666.
- Koterba AM, Coffman JR: Acute and chronic renal disease in the horse. *Comp Cont Educ Pract Vet* 1981; 3:S461-S469.
- Schott HC, Patterson KS, Fitzgerald SD et al: Chronic renal failure in 99 horses. *Proceedings of the 43rd Annual Convention of the American Association of Equine Practitioners*, pp 345-346, 1997.
- Tennant B, Kaneko JJ, Lowe JE et al: Chronic renal failure in the horse. *Proceedings of the 23rd Annual Convention of the American Association of Equine Practitioners*, pp 293-297, 1978.

CHAPTER 17.10

Renal Tubular Acidosis in Horses

MONICA ALEMAN
Davis, California

Renal tubular acidosis (RTA) is characterized by altered renal tubular function, resulting in a profound hyperchloremic metabolic acidosis with a normal anion gap. Renal tubular acidosis has been reported in humans, dogs, cats, and horses. In horses, RTA can be primary (idiopathic) or secondary to other concurrent disease. Although drug-induced RTA has not been reported in horses, some of the drugs implicated in the development of RTA in humans are used widely in horses. Such drugs are carbonic anhydrase inhibitors, potassium-sparing diuretics, β -adrenergic adrenoceptor

blockers, angiotensin-converting enzyme inhibitors, cyclosporin A, gentamicin, amphotericin B, trimethoprim/sulfamethoxazole, outdated tetracyclines, and non-steroidal antiinflammatory agents. Renal tubular acidosis should be considered as a differential diagnosis in horses that present with vague signs of depression, poor performance, anorexia, and weight loss. The key for its diagnosis is the finding of a profound hyperchloremic metabolic acidosis in a routine biochemical profile.

Horses can apparently have type I or II RTA or a combination of both. Type I RTA develops when the distal tubules

are unable to excrete hydrogen ions and therefore unable to acidify the urine. In type II RTA, the proximal tubules are unable to reabsorb bicarbonate, which results in tubular hydrogen retention and bicarbonate loss in the urine. No breed or sex predilection exists in horses, and to date no indication exists that RTA is an inherited condition. The mean age at onset of the disease is 7 years, but RTA can affect horses as young as 6 months. Type of diet or exercise level does not seem to have an effect on the development of RTA.

CLINICAL SIGNS

The most common clinical signs are depression, poor performance, weight loss, anorexia, weakness, decreased borborygmi, decreased fecal output, and mild colic. Other clinical signs include ataxia, mild dehydration, mild abdominal distention, dull hair coat, general unthrifty condition, tachypnea, and tachycardia that resolve upon the correction of the acidosis. Growth retardation has been described in children with RTA, but it has not been reported in horses.

LABORATORY FINDINGS

Blood gas analysis reveals a severe hyperchloremic metabolic acidosis with a low strong ion difference (SID). Serum chloride concentration can be 106 to 121 mEq/L, whereas plasma bicarbonate concentration is less than 13 mEq/L, plasma base deficit is greater than 15 mEq/L, and venous blood pH is less than 7.23. The serum SID is less than 30 mEq/L compared with the normal reference range of 38 to 44 mEq/L. The decreased excretion of hydrogen ions in patients with RTA results in acidosis. Hyperchloremia develops as a result of enhanced renal conservation of chloride consequent to bicarbonate loss. A strong association exists between the SID and the bicarbonate concentration before, during, and after the correction of the metabolic acidosis. In most cases, respiratory compensation for the metabolic acidosis is evident by a decreased P_{aCO_2} .

Some horses present with mild hyponatremia and moderate to marked hypokalemia. Potassium depletion develops from the combination of the decreased potassium intake because of anorexia, and the enhanced renal loss of potassium because of RTA, especially in patients with type II RTA. In the latter condition the high concentration of bicarbonate in the urine further increases urinary potassium excretion. Hyperbilirubinemia resulting from anorexia is a common finding in affected horses. Horses may have mild to moderate prerenal azotemia, but renal azotemia also may occur. Other abnormalities may include low urine osmolality and specific gravity, pigmenturia, glucosuria, and bacteriuria.

Affected horses generally have neutral to alkaline urine, but acid urine may be found in cases of RTA type II. Horses, being herbivores, normally maintain alkaline urine, making RTA identification difficult. Urine net charge (UNC) can be calculated from urine electrolyte concentrations as follows:

$$UNC = Na^+ + K^+ - Cl^-$$

The UNC is an indirect measurement of urine ammonium excretion. Horses with RTA tend to have a very low UNC

(lower than the reference range of +111 to +189 mEq/L). Higher concentrations of P_{CO_2} , T_{CO_2} , and HCO_3^- in urine, compared with blood, support a reabsorption defect corresponding to type II RTA. The fractional excretion (FE) of sodium is high in type I RTA, and the FE of potassium is low in type II RTA. Hyperphosphaturia has been documented in few horses with suspected type II RTA. A diagnosis of RTA type I is supported by failure of the urine to become acid after administration of ammonium chloride (0.1 g/kg in 6 L of water via nasogastric tube).

TREATMENT

Treatment of RTA consists of prompt correction of the acidosis by administration of large amounts of intravenous and oral sodium bicarbonate. Response to treatment largely depends on the rate of sodium bicarbonate administration. Half of the estimated bicarbonate deficit can be replaced safely with intravenous sodium bicarbonate over 6 to 12 hours, and the remaining deficit replaced with a combination of intravenous and oral sodium bicarbonate. Steady improvement in clinical signs is noted when plasma bicarbonate concentration increases to more than 20 mEq/L, and pH is greater than 7.3. Horses may require 3500 to 18,600 mEq of intravenous and oral sodium bicarbonate for the initial correction of the acidosis. The acidosis can be corrected relatively quickly (mean time of 3 days). The initial recommended oral dose is 100 to 150 grams every 12 hours, or 100 grams every 8 hours (1 gram of sodium bicarbonate = 11.9 mEq of sodium bicarbonate). Larger doses of bicarbonate can induce osmotic diarrhea, especially in anorectic horses. The diarrhea gradually resolves upon decreasing the dose. Close monitoring of acid-base and electrolyte status is required during therapy, especially if concurrent renal disease is present. Once the base deficit is corrected, continued oral supplementation of sodium bicarbonate for weeks to years may be required for the maintenance of a normal acid-base status in individual horses.

During the initial correction of the acidosis, intravenous and/or oral supplementation of potassium is necessary in most cases, as a moderate to marked hypokalemia develops, especially in horses that are already hypokalemic (serum $K^+ < 3$ mEq/L) before the correction of the acidosis. An initial intravenous dose of 20 to 30 mEq/L of potassium is recommended, but the rate of administration should not exceed 0.5 mEq/kg/hr. The intravenous potassium administration may be followed by oral administration of potassium chloride (30 g/500 kg PO q12h; 1 g potassium chloride = 13.4 mEq potassium).

Osmotic diarrhea may develop if oral potassium supplementation is combined with high doses of oral sodium bicarbonate. Once the horse's appetite returns, potassium supplementation can decrease gradually. Complications associated with rapid correction of the acidosis have not been reported. Treatment of any concurrent disease that may contribute to the development of RTA is important.

PROGNOSIS

Recurrence of RTA within days to years after initial recognition is not uncommon, especially if concurrent renal

disease is present. Reinstitution of therapy with sodium bicarbonate controls the clinical signs. Relapses upon discontinuation or decreasing the dose of sodium bicarbonate suggest that long-term treatment may be required in some cases. Some of the horses with evidence of renal disease may have multiple relapses. The short-term prognosis of horses with RTA is good. Although the long-term prognosis has not been well documented, some horses have been reported to recover completely, but continued problems can be anticipated if concurrent renal disease is present. Because the treatment and prognosis for both types of RTA in horses is similar, characterization of RTA is not as critical as in humans. Although the pathogenesis of RTA in horses remains uncertain, prompt recognition and early aggressive intravenous bicarbonate therapy followed

by long-term oral supplementation apparently are important to successful management.

Supplemental Readings

- Aleman M, Kuesis B, Harold CS et al: Renal tubular acidosis in horses (1980-1999). *J Vet Intern Med* 2001; 15:136-143.
- Clague A, Drause H: Broadsheet number 40: the diagnosis of renal tubular acidosis. *Pathology* 1997; 29:34-40.
- Rumbaugh GE, Carlson GP, Harrold D: Urinary production in the healthy horse and in horses deprived of feed and water. *J Am Vet Med Assoc* 1982; 43:735-737.
- Ziemer EL, Parker HR, Carlson GP et al: Renal tubular acidosis in two horses: diagnostic studies. *J Am Vet Med Assoc* 1987; 190:289-293.

CHAPTER 17.11

Once-Daily Aminoglycoside Dosing Regimens

RAYMOND J. GEOR
Guelph, Ontario, Canada
MARK G. PAPICH
Raleigh, North Carolina

The aminoglycoside antibiotics, particularly gentamicin and amikacin, are commonly used in the treatment of gram-negative bacterial infections in horses. In recent years it has been documented in human and animal patients that once-daily administration of the total dose of an aminoglycoside is more effective, and perhaps safer, than multiple daily dosing regimens. Sufficient pharmacokinetic data now exist from several equine studies in both adult horses and foals to support once-daily dosing regimens.

RATIONALE FOR ONCE-DAILY DOSAGE REGIMENS

A more complete understanding of the pharmacodynamics of the aminoglycosides, along with better knowledge of the mechanisms responsible for aminoglycoside toxicity, has established the foundation for once-daily aminoglycoside dosing regimens. This class of antibiotics exhibits both concentration-dependent bactericidal activity and a postantibiotic effect (PAE). The PAE is defined as persistent suppression of bacterial growth after drug concentrations have fallen below the minimum inhibitory concentration (MIC) of the invading bacteria. The PAE is also concentration-dependent, thus the higher the aminoglycoside concentration, the longer the PAE. The aminogly-

cides also demonstrate postantibiotic leukocyte enhancement (PALE), wherein exposure of bacteria to the drug results in enhanced leukocyte phagocytosis. The duration of the PALE is proportional to the aminoglycoside concentration. Therefore aminoglycoside dosing regimens should be designed to achieve high peak plasma concentrations of the drug (C_{MAX}) and, more specifically, a high ratio C_{MAX} to the MIC (C_{MAX}/MIC). These goals can be achieved by once-daily dosing, which has been referred to in some publications as *extended-interval aminoglycoside dosing* (EIAD). The longer interval between doses also provides a drug-free period that allows for reversal of adaptive resistance. Indeed studies in human patients with gram-negative infection have provided evidence that once-daily dosing may result in a more rapid clinical response than traditional dosing regimens.

Once-daily dosing may also lessen the risk of nephrotoxicity when compared with more conventional aminoglycoside dosing regimens (e.g., the total daily dose divided equally into three doses and administered at 8-hour intervals). Aminoglycoside-induced renal toxicity results from accumulation of these agents in the renal cortex. After filtration at the glomerulus, aminoglycoside antibiotics bind to phospholipids on the brush border of proximal tubular cells and are subsequently reabsorbed. Accumulation of aminoglycosides in proximal tubular cells inter-

disease is present. Reinstitution of therapy with sodium bicarbonate controls the clinical signs. Relapses upon discontinuation or decreasing the dose of sodium bicarbonate suggest that long-term treatment may be required in some cases. Some of the horses with evidence of renal disease may have multiple relapses. The short-term prognosis of horses with RTA is good. Although the long-term prognosis has not been well documented, some horses have been reported to recover completely, but continued problems can be anticipated if concurrent renal disease is present. Because the treatment and prognosis for both types of RTA in horses is similar, characterization of RTA is not as critical as in humans. Although the pathogenesis of RTA in horses remains uncertain, prompt recognition and early aggressive intravenous bicarbonate therapy followed

by long-term oral supplementation apparently are important to successful management.

Supplemental Readings

- Aleman M, Kuesis B, Harold CS et al: Renal tubular acidosis in horses (1980-1999). *J Vet Intern Med* 2001; 15:136-143.
- Clague A, Drause H: Broadsheet number 40: the diagnosis of renal tubular acidosis. *Pathology* 1997; 29:34-40.
- Rumbaugh GE, Carlson GP, Harrold D: Urinary production in the healthy horse and in horses deprived of feed and water. *J Am Vet Med Assoc* 1982; 43:735-737.
- Ziemer EL, Parker HR, Carlson GP et al: Renal tubular acidosis in two horses: diagnostic studies. *J Am Vet Med Assoc* 1987; 190:289-293.

CHAPTER 17.11

Once-Daily Aminoglycoside Dosing Regimens

RAYMOND J. GEOR
Guelph, Ontario, Canada
MARK G. PAPICH
Raleigh, North Carolina

The aminoglycoside antibiotics, particularly gentamicin and amikacin, are commonly used in the treatment of gram-negative bacterial infections in horses. In recent years it has been documented in human and animal patients that once-daily administration of the total dose of an aminoglycoside is more effective, and perhaps safer, than multiple daily dosing regimens. Sufficient pharmacokinetic data now exist from several equine studies in both adult horses and foals to support once-daily dosing regimens.

RATIONALE FOR ONCE-DAILY DOSAGE REGIMENS

A more complete understanding of the pharmacodynamics of the aminoglycosides, along with better knowledge of the mechanisms responsible for aminoglycoside toxicity, has established the foundation for once-daily aminoglycoside dosing regimens. This class of antibiotics exhibits both concentration-dependent bactericidal activity and a postantibiotic effect (PAE). The PAE is defined as persistent suppression of bacterial growth after drug concentrations have fallen below the minimum inhibitory concentration (MIC) of the invading bacteria. The PAE is also concentration-dependent, thus the higher the aminoglycoside concentration, the longer the PAE. The aminogly-

cides also demonstrate postantibiotic leukocyte enhancement (PALE), wherein exposure of bacteria to the drug results in enhanced leukocyte phagocytosis. The duration of the PALE is proportional to the aminoglycoside concentration. Therefore aminoglycoside dosing regimens should be designed to achieve high peak plasma concentrations of the drug (C_{MAX}) and, more specifically, a high ratio C_{MAX} to the MIC (C_{MAX}/MIC). These goals can be achieved by once-daily dosing, which has been referred to in some publications as *extended-interval aminoglycoside dosing* (EIAD). The longer interval between doses also provides a drug-free period that allows for reversal of adaptive resistance. Indeed studies in human patients with gram-negative infection have provided evidence that once-daily dosing may result in a more rapid clinical response than traditional dosing regimens.

Once-daily dosing may also lessen the risk of nephrotoxicity when compared with more conventional aminoglycoside dosing regimens (e.g., the total daily dose divided equally into three doses and administered at 8-hour intervals). Aminoglycoside-induced renal toxicity results from accumulation of these agents in the renal cortex. After filtration at the glomerulus, aminoglycoside antibiotics bind to phospholipids on the brush border of proximal tubular cells and are subsequently reabsorbed. Accumulation of aminoglycosides in proximal tubular cells inter-

feres with lysosomal, mitochondrial, and $\text{Na}^+/\text{K}^+/\text{ATPase}$ function. Importantly, sustained exposure of proximal tubular cells to the drug, as may occur with multiple daily dosing regimens (or prolonged use of the drug), results in greater accumulation of the drug and increased risk of nephrotoxicity. Animal studies have demonstrated that administration of the total daily dose of gentamicin as a single dose, which creates one high daily peak concentration of the drug, results in less renal injury than administration of the same daily dose divided into three doses per day or by continuous infusion.

Among other factors, aminoglycoside toxicity is related to persistently high plasma “trough” concentrations of the drug. The trough drug concentration is that concentration measured immediately before the next administered dose. With once-daily dosing, the 24-hour interval between doses allows adequate time for drug clearance, thus prolonging the time of a low trough concentration and limiting exposure of renal tubules to persistently high drug concentrations. Therefore the risk of nephrotoxicosis is decreased. It must be emphasized, however, that once-daily dosing does not obviate the risk of aminoglycoside nephrotoxicity and there have been cases of acute renal failure in horses receiving once-daily treatment with gentamicin. Regardless of the frequency of treatment, aminoglycoside therapy still carries risk of renal injury when compromised renal function is present because of a preexisting condition. To minimize the risk of aminoglycoside nephrotoxicosis and identify which animals may be predisposed, close clinical monitoring is required, particularly in critically ill patients such as hemodynamically unstable foals. These issues are further discussed below (see the section on clinical monitoring).

Beyond a potentially enhanced therapeutic efficacy and reduction of the incidence and severity of toxicosis, a once-daily dosing regimen offers practical advantages, particularly in the treatment of horses under field conditions.

CLINICAL APPLICATION

In general, gentamicin and amikacin are highly effective against gram-negative aerobes but have poor activity against gram-positive aerobes, with the exception of coagulase-positive *Staphylococcus* spp. Obligate anaerobes and facultative anaerobes under anaerobic conditions are also resistant to aminoglycosides. Amikacin is more active against a broader range of gram-negative bacteria, compared with gentamicin, and has lower susceptibility to inactivation by enzymes involved in plasmid-mediated resistance, the most common mechanism for bacterial resistance to aminoglycosides. On the other hand, gentamicin is inherently more active than amikacin against nonenteric organisms including *Actinobacillus* spp. and *Pasteurella* spp. Both aminoglycosides are generally used in combination with a β -lactam agent (e.g., potassium penicillin) to produce a synergistic broad-spectrum bactericidal effect. The β -lactam-associated inhibition of bacterial cell wall synthesis enhances the uptake of aminoglycosides into bacteria, which accounts for the synergy of this combination. These drugs should not be mixed in the same vial or syringe before dosing, however, because mixing these drugs produces *in vitro* inactivation of the aminoglycoside.

Rational aminoglycoside dosing regimens should be made on the basis of pharmacokinetic and pharmacodynamic information derived from populations of diseased foals and horses and the relationship of these data to clinical outcome. Unfortunately scant data are available about the horse and no consensus currently exists regarding the most appropriate aminoglycoside dosage regimens for foals and adults. It should be emphasized that the inherent variability in the distribution and clearance of the aminoglycosides, particularly in severely ill patients with altered systemic and renal hemodynamics and/or impaired renal function, likely precludes development of truly standardized dosing regimens that can be applied in all clinical situations. Nevertheless some general recommendations can be made on the basis of limited data in neonatal and adult horse populations. For example, it has been shown in human patients that doses of aminoglycosides that result in a C_{MAX} 8 to 10 times the MIC of the isolate confer optimal bactericidal effect. Thus once-daily aminoglycoside dosing regimens in horses also target a $C_{\text{MAX}}/\text{MIC}$ ratio of 8 to 10. In studies of healthy adult horses, this $C_{\text{MAX}}/\text{MIC}$ has been achieved with gentamicin doses of 6.6 to 8.8 mg/kg. Pharmacokinetic monitoring in adult horses with abdominal disease, however, demonstrated that gentamicin doses of 4 to 6.8 mg/kg were adequate to achieve the target $C_{\text{MAX}}/\text{MIC}$. Similarly, although some clinicians have recommended an amikacin dose of 20 mg/kg once daily, pharmacokinetic determinations as well as clinical experience have indicated that an amikacin dose of 10 to 14 mg/kg once daily is likely adequate in most adult horses.

Recent studies have drawn attention to potential problems with once-daily dosage regimens in infants. In human neonates, birth weight and postconceptional age are correlated to aminoglycoside clearance, with the latter correlated to glomerular filtration rate (GFR). Thus preterm and low birth weight infants have decreased aminoglycoside clearance. Because neonates also have a larger volume of distribution due to greater total body water, dosing regimens used in human neonates can often result in suboptimal peak antibiotic concentrations and potentially toxic trough concentrations. Thus updated regimens have been developed for newborn infants that allow for intervals of 24, 36, or 48 hours, depending on patient characteristics (e.g., age and weight). Compared with infants, however, foals are much more precocious at birth and ample data demonstrate that renal clearance in foals, even shortly after birth, is as high or higher than in adult horses. Therefore dosing interval adjustments need not be made for neonatal foals, unless renal clearance is impaired (discussed below), but the dose must be increased in comparison with that for adults to account for increased volume of distribution.

Aminoglycoside antibiotics are distributed throughout the extracellular fluid (ECF) space, and neonatal foals (<4 weeks of age) have larger total body water and ECF volume compared with adult horses. Accordingly, to avoid inadequate peak drug concentrations larger doses are recommended for neonatal foals. The transition to adult pharmacokinetic values occurs relatively rapidly; thus, adult doses can be used after 6 weeks of age. Table 17.11-1 shows recommended once-daily dosing regimens for gentamicin

Table 17.11-1

Pharmacokinetic Information and Dosing Regimens for Gentamicin and Amikacin in Horses

	$T_{1/2}$ (hr)	CL (ml/min/kg)	VD (L/kg)	C_{MAX} (μ g/ml)	Dose*
Amikacin					
Foal (<30 days old)	3.9†	1.84	0.52	40	20-25 mg/kg q24h
Adult	1.9	1.3	0.22	40	10 mg/kg q24h
Gentamicin					
Foal (<30 days old)	1.6	2.7	0.356	20	10-14 mg/kg q24h
Adult	1.7	1.5	0.18	20	4-6.8 mg/kg q 24h

$T_{1/2}$, Elimination half-life; CL, systemic clearance; VD, apparent volume of distribution (area method); C_{MAX} , desired peak plasma concentration.

*Dose listed can be administered either intravenously or intramuscularly (intramuscular absorption is nearly complete).

†Pharmacokinetic values are an approximation derived from several sources listed in the reference section and values listed represent averages from more than one study.

and amikacin in neonatal foals compared with adult horses, as well as suggested target peak and trough plasma drug concentrations.

The need for routine therapeutic drug monitoring (TDM) in foals and horses receiving aminoglycoside antibiotics is controversial. In humans, once-daily dosing regimens do not obviate the need for TDM as a means to optimize plasma drug concentrations. In human patients it has been shown that TDM is cost-effective because it decreases morbidity associated with nephrotoxicosis, and can reduce drugs costs. In equine patients, TDM can also be useful because a wide variation may exist in drug disposition among sick patients, especially in critically ill neonates. For example, the effective volume of distribution for aminoglycosides is often higher in septic patients or those with a "third-space" problem (e.g., uropertoneum or pleural effusion) necessitating a higher dose to produce the target peak plasma concentrations. Furthermore longer clearance times for gentamicin and amikacin have been observed in premature and full-term foals with hypoxemia, azotemia, and septicemia. Prolonged clearance is likely a consequence of renal hypoperfusion and decreased glomerular filtration rate. In these cases, a longer interdose interval may be needed to reduce the risk of nephrotoxicity. If TDM can identify cases in which the dose can be lowered, there are obvious cost benefits in equine medicine as well. Disadvantages of TDM in horses include the added expense and, particularly in field situations, the lack of access to a laboratory that can perform the drug assays within a reasonable time frame. Collection of serial blood samples after dosing in a field situation is also not often practical.

TDM is helpful to determine whether the target C_{MAX} has been achieved and whether drug clearance is adequate. To perform TDM, either a single sample can be collected 30 minutes to 1 hour postdosing for an estimate of the peak drug concentrations (C_{MAX}), or two or three samples can be collected at 1- or 2-hour intervals to identify the slope of the elimination curve. Analysis of a series of points requires linear regression analysis and calculation of the slope of the curve plotted on a logarithmic axis (Figure 17.11-1). From the elimination curve, estimates of

clearance, volume of distribution, and half-life ($T_{1/2}$) are possible. These approaches are illustrated in Figure 17.11-1. Alternatively, a single trough sample can be collected immediately prior to the next scheduled dose. However, as illustrated in Figure 17.11-1, drug concentration in trough samples are often below the limit of detection of the assay, unless there is impaired clearance and drug accumulation. In situations in which TDM is not available, repeated evaluation of renal function is recommended during aminoglycoside therapy (see section on clinical monitoring).

When an aminoglycoside dosing regimen is selected, attention must be paid to the site of infection, susceptibility of the pathogen, severity of illness, and the patient's renal function. For example, the aminoglycoside antibiotics are poorly distributed to the lung and may not be the most appropriate antimicrobial selection for treatment of pulmonary infections. Next, in a pyogenic infection, especially an abscess, aminoglycosides may be inactivated by cellular debris. The immune competence of the patient also is important because neutrophil activity appears to be an important component of the PAE, and a once-daily dosing regimen in neutropenic patients may not be advisable. In these patients, use of a more conventional dosing regimen or the addition of a synergistic β -lactam antibiotic may be advisable. Finally, when aminoglycoside antibiotics are needed in patients with compromised renal function, the clinician can monitor a series of plasma drug concentrations (e.g., 1, 2, and 4 hours after administration) to determine drug clearance (which should approximate GFR) or measure a single sample at the end of a dosing interval to identify whether the trough concentrations are below the toxic range. These two measures are safeguards against exacerbation of renal damage.

CLINICAL MONITORING

Anecdotal evidence suggests that nephrotoxicity is the most common adverse effect of aminoglycoside use in foals and horses, whereas ototoxicity and neuromuscular dysfunction have not been reported. For obvious reasons, however, use of aminoglycoside antibiotics is contraindi-

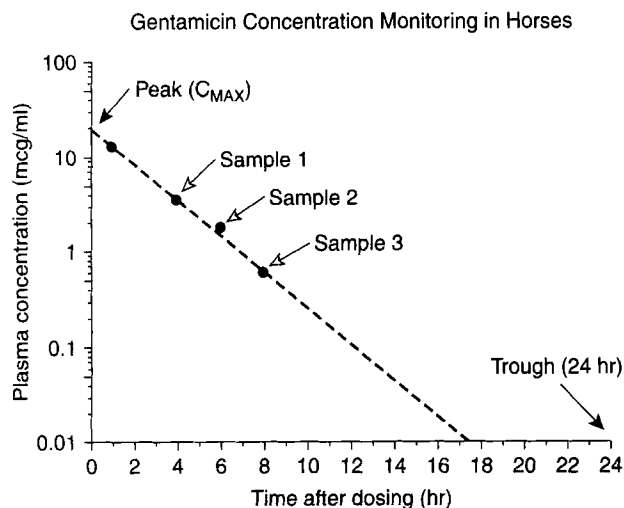


Figure 17.11-1 Gentamicin plasma concentration monitoring in horses. In this example plasma samples were collected from an adult horse given 4 mg/kg IV to determine gentamicin concentrations. Three strategies for plasma concentration monitoring are illustrated. (1) A single concentration, collected one hour after drug administration represents an approximate peak (C_{MAX}). The C_{MAX} in this case at 1 hour was 13 $\mu\text{g}/\text{ml}$, which would be adequate (i.e., $8\text{--}10 \times$ the MIC) for organisms with an MIC of approximately 1.3 $\mu\text{g}/\text{ml}$, or less. (2) A sample collected immediately before the next dose (24 hours) represents the trough. The trough in this example is below the limit of detection and indicates that the risk of renal toxicity is low. If an elevated trough concentration were identified, it would increase the risk of nephrotoxicosis. (3) To estimate the half-life ($T_{1/2}$) and clearance, a series of three samples can be collected approximately 1 to 2 hours apart, represented by samples 1, 2, and 3 collected at 4, 6, and 8 hours, respectively. In this example, the three samples were used to estimate the half-life, which was 1.6 hours (normal for an adult horse). The advantage of collecting a series of three samples is that peak and trough concentrations can be extrapolated by extending the straight line to the intercepts (dashed line) to determine the true peak and trough concentrations. The true C_{MAX} in this example (y-axis intercept) was approximately 20 $\mu\text{g}/\text{mL}$. The apparent volume of distribution also can be calculated with this approach from the volume of distribution (VD) = dose/ C_{MAX} . In this example, the VD was approximately 0.2 L/kg (normal for an adult horse). The systemic clearance, calculated from the formula: Systemic clearance = $(0.693 \times VD)/T_{1/2}$ was 1.44 mL/kg/min (also normal for an adult horse).

cated in animals with botulism. The risk of aminoglycoside-induced renal injury is related to the duration of therapy, the total dose delivered to the patient during the course of therapy, and use of concurrent nephrotoxic drugs (e.g., nonsteroidal antiinflammatory agents). Preexisting renal dysfunction, hypovolemia, sepsis, endotoxemia, and hypokalemia also increase the risk of nephrotoxicity (see Chapter 17.8: "Acute Renal Failure").

All patients that receive prolonged (>5 days) aminoglycoside therapy should be monitored for evidence of nephrotoxicity. In addition, the impact of concurrent risk

factors should be minimized. For example, adequate hydration should be maintained and other nephrotoxic agents (particularly the nonsteroidal antiinflammatory drugs) should be used at the lowest effective dose or avoided altogether. To monitor for aminoglycoside nephrotoxicity, serum creatinine (Cr) concentration should be measured every 2 to 3 days during treatment. A population pharmacokinetic study in horses showed that Cr concentration is the best predictor of gentamicin clearance compared with other variables. If evidence of renal dysfunction develops (a 0.3 mg/dl or greater increase in Cr concentration), the clinician should consider discontinuing therapy or increasing the dosing interval. It should be recognized, however, that Cr concentration accounts for only 40% of the variability in the clearance of gentamicin in horses with sepsis. Therefore monitoring of plasma drug concentrations may be a more sensitive guide to aminoglycoside clearance. Decreased clearance and increased trough concentrations would also be early indicators of renal dysfunction.

Serial urinalysis is a more sensitive method to monitor nephrotoxicity when compared with measurement of Cr concentration. Changes in urine sediment, enzymuria, mild proteinuria, glucosuria, and decreased concentrating ability may develop several days before an increase in Cr concentration. An increase in the ratio of urinary γ -glutamyl transferase (GGT) activity to urinary Cr (uCr) concentration (see Chapter 17.1: "Examination of the Urinary System") reflects damage to the brush border of proximal tubular epithelial cells and a urinary GGT/(uCr \times 0.01) value greater than 25 has been suggested to be an early indicator of nephrotoxicity. In four of five research ponies that were given toxic doses of gentamicin (20 mg/kg IV, q8hr), urinary GGT/(uCr \times 0.01) values exceeded 100 two to four days before increases in serum Cr were detected but considerable variation between ponies was observed. These findings illustrate several important points with regard to monitoring for aminoglycoside-induced nephrotoxicity in equine patients. First, the risk of nephrotoxicity varies considerably between horses. Second, renal tubular injury precedes increases in Cr concentration by several days. Third, minor increases in the urinary GGT:uCr ratio should be interpreted with caution.

Supplemental Readings

- Chattopadhyay B: Newborns and gentamicin—how much and how often? *J Antimicrob Chemother* 2002; 49:13-16.
- Green SL, Conlon PD, Mama K et al: Effects of hypoxemia and azotemia on the pharmacokinetics of amikacin in neonatal foals. *Equine Vet J* 1992; 24:475-479.
- Maglio D, Nightingale CH, Nicolau DP: Extended interval aminoglycoside dosing: from concept to clinic. *Int J Antimicrob Agents* 2002; 19:341-348.
- Martin-Jimenez T, Papich MG, Riviere JE: Population pharmacokinetics of gentamicin in horses. *Am J Vet Res* 1998; 59:1589-1598.
- Papich MG: Current concepts in antimicrobial therapy for horses. *Proceedings of the 47th Annual Convention of the American Association of Equine Practitioners*, pp 99-102, 2001.
- Tudor RA, Papich MG, Redding WR: Drug disposition and dosage determination of once daily administration of gentamicin sulfate in horses after abdominal surgery. *J Am Vet Med Assoc* 1999; 115:503.

CHAPTER 17.12

Hematuria

HAROLD C. SCHOTT II

East Lansing, Michigan

Hematuria can be the presenting complaint for a variety of disorders of the urinary tract. The problems that cause hematuria can range from relatively minor disorders to more severe disease processes that may result in life-threatening hemorrhage. Hematuria throughout urination is consistent with hemorrhage from the kidneys, bladder, or ureters, whereas hematuria at the beginning or end of urination may be associated with lesions in the distal or proximal urethra, respectively. A thorough diagnostic evaluation that includes endoscopy, ultrasonography, rectal palpation, physical examination, and analyses of blood and urine is usually rewarding in establishing the source and cause of urinary tract hemorrhage.

CYSTITIS AND PYELONEPHRITIS

Although relatively uncommon in horses, urinary tract infections may result in hematuria. In addition to infection of the upper urinary tract, fever, weight loss, and partial anorexia may be additional presenting complaints, whereas horses with cystitis generally manifest stranguria or pollakiuria.

The diagnostic evaluation should include the tests mentioned previously along with submission of a urine sample for bacterial culture. Occasionally horses may have an anatomic bladder defect or bladder paralysis that predisposes them to cystitis. Treatment consists of appropriate antimicrobial therapy and treatment of predisposing causes (see Chapter 17.2: "Urinary Incontinence").

UROLITHIASIS

The presence of uroliths at any level of the urinary tract may cause mucosal irritation and hemorrhage, resulting in hematuria. Affected horses also typically show signs of renal colic or painful urination indicated by stranguria or pollakiuria, especially with uroliths in the bladder or urethra. Rectal examination, passage of a urinary catheter, cystoscopy, or ultrasonography usually help to establish the diagnosis. Furthermore, urolithiasis can be accompanied by urinary tract infection; thus all horses with urolithiasis should additionally be evaluated for infection. Successful treatment consists of appropriate antimicrobial therapy and surgical removal of the urethral or bladder stones; however, recurrence is possible. Nephroliths and ureteroliths carry a more guarded prognosis, especially with bilateral disease that results in chronic renal failure. Nephrectomy may be an effective treatment option in horses with unilateral disease.

URINARY TRACT NEOPLASIA

Neoplasia of the kidneys, ureters, bladder, and urethra may result in hematuria. Renal adenocarcinoma and squamous cell carcinoma are the neoplasms most frequently reported to affect the upper and lower urinary tract, respectively. Rectal, physical, laboratory, cystoscopic, and ultrasonographic examinations usually help to detect the neoplasm. Treatment is usually unsuccessful unless a benign neoplasm can be removed by unilateral nephrectomy or a squamous cell carcinoma can be removed by partial resection of the bladder or penis. Neoplasms affecting the distal urethra, which are usually squamous cell carcinoma or sarcoid, may also be amenable to surgical resection in combination with local application of antineoplastic agents.

DRUG TOXICITY

Nephrotoxicity, particularly as a result of administration of nonsteroidal antiinflammatory drugs (NSAIDs; especially phenylbutazone) may result in moderate to severe hematuria. The historic or current use of nephrotoxic medications supports this diagnosis, and discontinuation of the nephrotoxic agent and supportive care are the appropriate treatments.

URETHRAL DEFECTS

Although a recognized cause of hemospermia in stallions, defects or tears of the proximal urethra at the level of the ischial arch are a more recently described cause of hematuria in geldings. Because the defects are difficult to detect without use of high-resolution videoendoscopic equipment, it is likely that lesions have been missed in previous reports of urethral bleeding. Consequently, hematuria has been attributed to urethritis or hemorrhage from "varicosities" of the urethral vasculature. Because the vasculature underlying the urethral mucosa becomes quite prominent when the urethra is distended with air during endoscopic examination, especially in the proximal urethra, it is easy to suspect that hemorrhage can arise from an apparent urethritis or urethral varicosity.

Urethral defects or tears typically result in hematuria at the end of urination in association with urethral contraction. Affected horses generally void a normal volume of urine that is not discolored. At the end of urination, affected geldings experience a series of urethral contractions that result in passage of squirts of bright red blood. Occasionally a smaller amount of darker blood may be passed at

the start of urination. In most instances the condition does not appear painful or result in pollakiuria. Interestingly, the majority of affected geldings have been Quarter Horses or Quarter Horse crosses that have been free of other complaints. Treatment with antibiotics for suspected cystitis or urethritis has routinely been unsuccessful, although hematuria has resolved spontaneously in some cases.

Examination of affected horses is often unremarkable. In comparison, horses with hematuria caused by neoplasms involving the distal urethra or penis usually present with additional complaints such as pollakiuria, a foul odor to the sheath, or presence of a mass in the sheath or on the penis. With urethral defects, laboratory analysis of blood reveals normal renal function, although mild anemia is an occasional finding. Urine samples collected in midstream or by bladder catheterization appear grossly normal. Urinalysis may have normal results or an increased number of red blood cells may appear on sediment examination, a finding that also results in a positive reagent strip result for blood. Bacterial culture of urine yields negative results.

The diagnosis is made through endoscopic examination of the urethra during which a lesion is typically seen along the dorsocaudal aspect of the urethra at the level of the ischial arch (Figure 17.12-1). With hematuria of several weeks' duration, the lesion appears as a fistula communicating with the vasculature of the corpus spongiosum penis, the cavernous vascular tissue surrounding the urethra. External palpation of the urethra in this area is usually unremarkable but can help to localize the lesion, because external digital palpation can be seen through the endoscope as movements of the urethra.

Although the pathophysiology of this condition remains unclear, the defect has been hypothesized to be the result of a "blowout" of the corpus spongiosum penis into the urethral lumen. Contraction of the bulbospongiosus muscle during ejaculation causes a dramatic increase in pressure in the corpus spongiosum penis, which is essen-

tially a closed vascular space during ejaculation. The bulbospongiosus muscle also undergoes a series of contractions to empty the urethra of urine at the end of urination; thus, the defect into the urethra may develop by a similar mechanism in geldings. Once the lesion has been created, it is maintained by bleeding at the end of each urination, and the surrounding mucosa heals by formation of a fistula into the overlying vascular tissue. An explanation for the consistent location along the dorsocaudal aspect of the urethra at the level of the ischial arch has not been documented but may be related to the anatomy of the musculature supporting the base of the penis and an enlargement of the corpus spongiosum penis in this area. Furthermore, a narrowing of the lumen of the urethra occurs at the distal extent of the ampullar portion of the urethra, which may also contribute to the location of the defects. An anatomic predisposition in Quarter Horses has not been documented but could be proposed on the basis of an apparent increased risk in this breed.

Because hematuria may resolve spontaneously in some affected geldings, no treatment may be initially required. If hematuria persists for more than a month or if significant anemia develops, a temporary subischial urethrotomy has been successful in a number of affected geldings. With sedation and epidural or local anesthesia, a vertical incision is made down to a catheter that has been placed in the urethra. The surgical wound requires several weeks to heal, and moderate hemorrhage from the corpus spongiosum penis is apparent for the first few days after surgery. Additional treatment consists of local wound care and prophylactic antibiotic treatment, typically a trimethoprim/sulfonamide combination, for 7 to 10 days. Hematuria should resolve within a week after this procedure. Treatment by incising into the corpus spongiosum penis but not into the urethral lumen has also been successfully employed. This treatment option provides support for the "blowout" etiology and lessens the risk of urethral stricture formation.

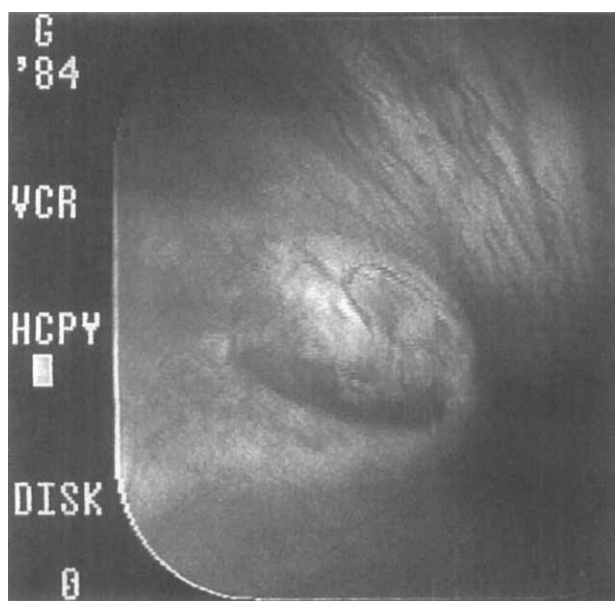


Figure 17.12-1 Urethral defect in a gelding that resulted in hematuria at the end of urination. Dorsocaudal aspect of urethra is on the left.

IDIOPATHIC RENAL HEMATURIA AND RENAL VASCULAR ANOMALIES

Macroscopic hematuria, often accompanied by passage of blood clots and development of life-threatening anemia, has been observed in a limited number of adult horses. A similar condition of severe and recurrent renal hemorrhage, unassociated with trauma or other obvious causes of hemorrhage, has been described in humans and dogs as idiopathic renal hematuria or benign essential hematuria. In these species, hematuria is more commonly a unilateral than a bilateral problem, similar to that which has been observed in the few affected horses. The pathophysiology remains poorly understood, but in humans the macroscopic hematuria has been associated with immune-mediated glomerular damage caused by acute postinfectious glomerulonephritis, membranoproliferative glomerulonephritis, and immunoglobulin A nephropathy or Berger's disease. In other instances, a vascular anomaly has been detected. Although hematuria has been recognized with systemic disease in horses, patients affected with idiopathic renal hematuria appear to have spontaneous, severe hematuria in the absence of other signs of disease. Urinary tract infection or lithiasis has not been detected, and the magnitude of

hematuria has resulted in death or the need for repeated blood transfusions in several horses.

The diagnosis of idiopathic renal hematuria is made by exclusion of systemic disease, alterations in hemostasis, and other causes of hematuria. Physical examination may reveal tachycardia, tachypnea, and pale membranes consistent with acute blood loss. Rectal palpation may reveal an enlarged, irregular bladder resulting from the presence of blood clots. Azotemia has not been detected unless substantial hemorrhage has occurred, and urinalysis typically shows only hematuria and proteinuria. Endoscopic examination is important to document that hematuria is originating from the upper urinary tract. Blood clots can be seen exiting the ureters in affected horses. Endoscopy also helps determine whether hemorrhage is unilateral or bilateral. Repeated examinations may be required to answer the latter question. Ultrasonographic imaging may be within normal limits or may reveal loss of parenchymal detail (i.e., loss of the corticomedullary junction). Ultrasonographic imaging is necessary to rule out nephrolithiasis or ureterolithiasis and may occasionally reveal a distended vascular space or renal vascular anomaly as the cause of hematuria. Renal biopsy may help to document immunologic glomerular injury, but the significance of such results is not well understood at this time.

Treatment for idiopathic hematuria consists of supportive care for acute blood loss, including blood transfusions. The condition may be self-limiting in some patients; thus treatment is warranted. With severe and recurrent hematuria of unilateral renal origin or when a vascular anomaly is detected on ultrasonographic imaging, a nephrectomy may be indicated.

Over the past decade, this author has evaluated seven horses and consulted with veterinarians on six additional cases of apparent idiopathic renal hematuria. Although both sexes and a range of age and breeds (including a mammoth donkey and a mule) have been affected, 6 of the 13 horses were Arabians—this fact suggests a possible breed predisposition. Despite the presence of active renal hemorrhage, results of physical examination were often unremarkable unless anemia was severe (packed cell volume <15%). Similarly, results of complete blood counts and serum biochemistry profiles usually reflected only hemorrhage (anemia) and stress (mature neutrophilia, mild hyperglycemia). In three horses with repeated bouts of hemorrhage or concurrent use of nephrotoxic medications (NSAIDs and/or gentamicin), mild azotemia was detected. Results of coagulation profiles were normal in the few cases in which they were performed, although platelet counts tended to be toward the lower end of the normal range. Cystoscopic examination revealed unilateral hematuria in all patients but the problem subsequently developed in the contralateral kidney in two mares subjected to a nephrectomy. Nine horses either suffered a fatal hemorrhage or were destroyed within 3 months of the initial observed bout of hematuria. One horse developed chronic renal failure after a 2-year course of intermittent hematuria, prompting a decision for euthanasia. Twelve horses either died or were euthanized within 2 years of initial hemorrhage and one stallion has remained free of renal bleeding for 3 years after unilateral nephrectomy. Unfortunately, only a few horses have been subjected to necropsy examination. Dilatation of the renal pelvis with blood clots has been found along with histologic changes

including evidence of prior infarcts (not apparently associated with the hemorrhage), but minimal light microscopic evidence of glomerular disease has been detected. In two cases the inner medullary collecting ducts were filled with blood, suggesting leakage from the vasculature (a possible microvascular disease) at this level.

EXERCISE-ASSOCIATED HEMATURIA

Exercise is accompanied by increased filtration of red blood cells and protein across the glomerular barrier in a high percentage of human and equine athletes. Typically, the hematuria is microscopic, but gross discoloration of urine may occasionally be observed. Gross hematuria may more commonly be a consequence of bladder erosions that may be traumatically induced by the abdominal contents pounding the bladder against the pelvis during exercise. Detection of focal bladder erosions or ulcers with a contrecoup distribution and a history of emptying the bladder immediately before the exercise bout are characteristic of this problem. A diagnosis of exercise-associated hematuria should be made after diagnostic evaluation has been performed to rule out other causes of hematuria, such as presence of a cystolith.

PIGMENTURIA ASSOCIATED WITH SYSTEMIC DISEASE

With any systemic disease that may lead to alterations in hemostasis or vascular permeability, hematuria or hemoglobinuria may develop. Discolored urine may be accompanied by a degree of nephrotoxicity because of interaction of iron ions of the heme molecules with proximal tubular epithelial cells. With transient pigmenturia, as with exercise-associated hematuria, changes in renal function may not be apparent, but with more severe disease processes and hemolysis acute renal failure may develop. Hemolysis and hemoglobinuria may also be recognized with liver disease or immune-mediated hemolytic anemias consequent to infection with *Streptococcus equi* or to drug treatments. Conditions accompanied by extensive rhabdomyolysis may also result in pigmenturia. Assessment of muscle enzyme activity in these cases usually helps to establish myoglobin as the most likely cause of pigmenturia.

Supplemental Readings

- Behm RJ, Berg IE: Hematuria caused by renal medullary crest necrosis in a horse. *Comp Cont Educ Pract Vet* 1987; 9:698-703.
- Fischer AT, Spier S, Carlson GP et al: Neoplasia of the urinary bladder as a cause of hematuria. *J Am Vet Med Assoc* 1985; 186(12):1294-1296.
- Kaufman AC, Barsanti JA, Selcer BA: Benign essential hematuria in dogs. *Comp Cont Educ Pract Vet* 1994; 16:1317-1323.
- Lloyd KCK, Wheat JD, Ryan AM et al: Ulceration in the proximal portion of the urethra as a cause of hematuria in horses: four cases (1978-1985). *J Am Vet Med Assoc* 1989; 194:1324-1326.
- Schott HC, Hines MT: Severe urinary tract hemorrhage in two horses [letter to editor]. *J Am Vet Med Assoc* 1994; 204:1320.
- Schott HC, Hodgson DR, Bayly WM: Haematuria, pigmenturia and proteinuria in exercising horses. *Equine Vet J* 1995; 27:67-72.
- Schumacher J, Varner DD, Schmitz DG et al: Urethral defects in geldings with hematuria and stallions with hemospermia. *Vet Surg* 1995; 24:250-254.

CHAPTER 17.13

Uroperitoneum

RACHAEL CONWELL

Chalfont Saint Giles, Bucks, United Kingdom

Uroperitoneum involves leakage of urine in to the peritoneal cavity. This can occur via the urachus, bladder, or ureters. It is a condition seen most commonly in the neonate and usually is associated with rupture of the urinary bladder. Tears are found more frequently in the dorsal wall of the bladder. This is due to a natural weakening in this area, although tears also can occur in the ventral wall.

The male foal is considered classically to be at increased risk of developing a ruptured bladder, although some studies have shown no gender predilection for the condition. The rupture is suspected to occur during parturition, when the effects of compression of a full bladder are exacerbated by the long, narrow urethra in the male, leading to increased intramural pressure. The female, by comparison, has a much shorter and wider urethra, so pressure is dissipated more readily as urine flows out of the bladder. Disruption of the urinary tract can occur spontaneously in hospitalized, particularly septic or debilitated, neonates. The etiology in these cases is a focal necrotic cystitis. Congenital defects are uncommon and, when they do occur, usually are associated with the ureters. Ectopic ureter is the most common anomaly seen, with agenesis rarely reported.

Urachal disease typically occurs secondary to infection and necrosis. This results in either uroperitoneum or subcutaneous leakage of urine, which causes ventral abdominal swelling. Uroperitoneum also can occur after avulsion of the urachus after external trauma or strenuous exercise.

In the adult horse, uroperitoneum has been seen in mares after rupture of the bladder or, more rarely, the ureter, after dystocia or prolonged parturition. Bladder rupture may be caused by compression and confusion of the bladder between the foal and the pelvic brim or occlusion of the urethra by the foal in the pelvis. Ureteral damage is thought to occur with trauma to the broad ligament of the uterus. Dehiscence of the bladder repair after surgical removal of calculi also can result in uroperitoneum.

CLINICAL SIGNS

The clinical signs are variable and usually minimal in the early stages. Affected foals tend to be normal at birth, with age at onset of signs depending on the size and location of the tear. Foals with large tears may present within the first 48 hours, whereas those with small tears may not present until up to 7 days of age. Septic foals with bladder rupture secondary to ischemic necrosis of the bladder wall also present in the older age group.

The initial signs are nonspecific and can be confused with those of septicemia or gastrointestinal disease. Foals appear dull, depressed, and anorexic and may show mild

abdominal pain. Stranguria or pollakiuria can be variable and some foals may urinate normally, although anuria is rare. Straining to urinate can be mistaken for straining associated with meconium impaction, and the two conditions can occur concurrently. As the condition progresses, abdominal distention becomes more apparent; this can lead to respiratory compromise.

Affected adults show signs similar to foals, namely depression, anorexia, colic, abdominal distention, and increased respiratory effort.

DIAGNOSIS

The signalment of the foal and clinical signs may be suggestive of uroperitoneum. However, particularly in the early stages, or when multisystemic disease processes complicate the condition, a thorough diagnostic workup is essential.

Hematologic values tend to be normal, unless the foal is also septic. In these cases, a leukopenia, possibly with toxic neutrophils, generally is seen. Electrolyte derangements are common. In comparison with plasma, urine has low levels of sodium and chloride and high levels of potassium, urea, and creatinine. The peritoneal lining allows relatively free movement of electrolytes and small molecules, leading to expansion of the extracellular volume and equilibration with the plasma. Therefore blood clinicopathologic values reveal hyponatremia, hypochloremia, hyperkalemia, and elevated blood urea nitrogen and creatinine. Foals may be acidotic, which is identified by blood gas analysis. The changes can vary, particularly in hospitalized neonates already receiving intravenous fluids. In these cases, serum creatinine is the value least affected by the fluid therapy.

Analysis of peritoneal fluid can be helpful. Usually a copious amount is present, and occasionally calcium carbonate crystals may be seen on direct microscopic examination. Creatinine is a large molecule that diffuses poorly across the peritoneal lining, in comparison with the smaller urea. Therefore levels in the peritoneal fluid remain much higher than in the serum. A peritoneal:serum creatinine ratio of greater than 2 is considered diagnostic for uroperitoneum.

Severe electrolyte disturbances can result in neurologic signs. Hyponatremia may lead to hyperesthesia and seizures. Hyperkalemia can cause bradycardia, third-degree atrioventricular node blockade and arrhythmias, including ventricular fibrillation. ECG findings with hyperkalemia include reduced P wave amplitude and increased P wave duration, prolonged P-R interval, increased duration of QRS complex, short QT interval, and increased T wave amplitude.

Injection of a sterile dye solution into the bladder, via a urinary catheter, identifies the presence of a tear because

the dye is found in the peritoneal fluid. Methylene blue and fluorescein are suitable dyes. However, this does not locate the site of the tear.

Abdominal radiography can be useful but has been superseded to some extent by the use of ultrasonography. Plain radiographs show loss of contrast of the abdominal organs because of fluid in the abdomen. Retrograde contrast cystography, using a 10% solution of water-soluble contrast media, may help to identify the site of a bladder rupture. The bladder must be distended adequately with the contrast material. This technique does not identify ureteral defects.

Abdominal ultrasonography shows increased fluid in the peritoneal cavity. The ruptured bladder develops a collapsed, infolding appearance, and in some cases identification of the site of the defect in the bladder wall is possible. This can be aided by introduction of an agitated saline sample directly in to the bladder via a catheter. Air bubbles can be seen leaving the bladder into the peritoneal cavity. Urachal tears may result in intraabdominal or subcutaneous accumulation of urine, with abscess formation in the latter case. This also can be differentiated ultrasonographically.

Identification of any co-existing gastrointestinal, respiratory or renal problems also is important, particularly in the septic neonate, because these conditions may affect the management and prognosis. The immunoglobulin status also should be assessed because the majority of septicemic foals have failure of passive transfer.

In the adult horse, endoscopy of the bladder can allow direct visualization of the site of the tear. Abdominal laparoscopy also may be considered.

TREATMENT

Uroperitoneum is a medical emergency. Correction of the electrolyte disturbances is the primary aim because, if untreated, they can be fatal. This is achieved by a combination of intravenous fluid therapy and removal of the abdominal fluid. Appropriate fluids include 0.9% or 1.8% saline. The use of fluids containing potassium is not recommended. The addition of 5% dextrose or sodium bicarbonate may be necessary for cases with severe hyperkalemia, to promote cellular uptake of the potassium. Bicarbonate also may be necessary to correct severe metabolic acidosis.

Abdominal drainage should be performed slowly while giving the intravenous fluids. This is especially important in the adult, because removal of large volumes of fluid from the abdomen can result in hypovolemic shock after redistribution of blood to the abdominal vascular beds. Drainage can be achieved using peritoneal dialysis catheters, teat canulas, Foley catheters, or intravenous catheters. As the abdominal distention resolves, cardiopulmonary function also improves.

Small tears can heal without surgical repair and with the use of an indwelling urinary catheter. In the majority of

cases, surgical repair is necessary; correction of electrolyte disturbances is extremely important before consideration of induction of general anesthesia. General recommendations are that potassium levels should be less than 5.5 mEq/L before anesthesia induction. Repair of the bladder has been performed successfully in a standing adult mare with the aid of epidural anesthesia and sedation.

Broad-spectrum antibiotics always should be given preoperatively, particularly when an abdominal catheter is used before surgery or a urachus or umbilicus is infected. Sodium penicillin or ampicillin is preferable to avoid additional potassium administration. They are used generally in combination with an aminoglycoside such as gentamicin or amikacin. Whether a urinary tract rupture alters the renal clearance of aminoglycosides is unknown. However, this is unlikely to present a clinical problem in a foal that is receiving adequate fluid therapy. Ceftiofur is another suitable alternative. Use of antibiotics is continued for 7 to 10 days after surgery.

Postoperatively, a urinary catheter often is sutured in place to prevent overfilling of the bladder and subsequent increased pressure on the site of bladder repair. The catheter can be removed after 1 to 3 days.

PROGNOSIS

Repair of bladder rupture generally has a favorable outcome, providing no additional complications, such as septicemia, exist. Foals with a positive sepsis score have a poorer prognosis for survival.

The main problems occur as a result of electrolyte disturbances in the perioperative period or dehiscence of the bladder repair in the postoperative period. Peritonitis is rare in foals because of a poorly developed polymorphonuclear system and occurs more commonly in adults. Early diagnosis and early treatment are vital for a successful outcome in all cases of uroperitoneum.

Supplemental Readings

- Adams R, Koterba AM, Cudd TC et al: Exploratory celiotomy for suspected urinary tract disruption in neonatal foals: a review of 18 cases. *Equine Vet J* 1988; 20:13-17.
- Hackett RP: Rupture of the urinary bladder in neonatal foals. *Comp Cont Educ Prac Vet* 1984; 6:S488-S494.
- Hardy J: Uroabdomen in foals. *Equine Vet Educ* 1998; 10:21-25.
- Jean D, Marcoux M, Louf C-F: Congenital bilateral distal defect of the ureters in a foal. *Equine Vet Educ* 1998; 10:17-20.
- Jones PA, Sertich PS, Johnston JK: Uroperitoneum associated with ruptured urinary bladder in a postpartum mare. *Aust Vet J* 1996; 74:354-358.
- Kablak KA, Embertson RM, Bernard WV et al: Uroperitoneum in the hospitalised equine neonate: retrospective study of 31 cases, 1988-1997. *Equine Vet J* 2000; 32:505-508.
- Worth LT, Palmer JE, Bentz B: What is your diagnosis? *J Am Vet Med Assoc* 1997; 210:1601-1602.

APPENDICES

APPENDIX 1

Table of Drugs, Approximate Doses

N. EDWARD ROBINSON
East Lansing, Michigan

Name of Drug	Dose	Route
Acepromazine	0.03-0.066 mg/kg for sedation	IM
	0.033-0.055 mg/kg followed by 0.055-0.066 mg/kg butorphanol	IV
	0.04 mg/kg followed by 0.6 mg/kg meperidine	IV
	0.02-0.055 mg/kg q8h for α -adrenoceptor blockade	IM
Acetazolamide	2.2 mg/kg q12h-q6h	PO
Acetylcysteine (10%)	2-5 ml/50 kg q6h	Aerosol
	10% topical solution q1-4h	Ophthalmic
Aclometasone	0.05%	Topical
Acyclovir 3%	5-10 mg/kg q8h	PO
	q3-4h	Ophthalmic
Adrenocorticotrophic hormone	0.26 mg q8-12h (depot preparation)	IM
Albendazole	0.125 mg/foal (tests adrenal function of premature foals)	IV
	25 mg/kg q12h for 5 days for <i>Dictyocaulus arnfieldi</i>	PO
	50 mg/kg q12h for 2 days for <i>Strongylus vulgaris</i> larvae	PO
	4-8 mg/kg q12h for 1 month for <i>Echinococcus</i>	PO
Albuterol	1-2 μ g/kg	Inhalation
Alfaprostol	3 mg/450 kg for luteolysis; 2 doses 14-18 days apart	IM
Allopurinol	5 mg/kg	IV
alpha-tocopherol	1.5-4.4 mg/kg q24h	PO
Altrenogest	0.044 mg/kg q24h for 8-12 days; for estrus	PO
	synchronization follow with luteolytic dose	
	of prostaglandin F ₂ α	
	0.044 mg/kg to prevent aggression	PO
Aluminum hydroxide	0.44 mg/kg q24h for pregnancy maintenance	PO
	200-250 ml q8h (antacid)	PO
	60 mg/kg	PO
Amikacin	3.5-7.5 mg/kg q12h to q6h	IM or SQ
	15-20 mg/kg q24h	IM or SQ
	1-10 mg/kg q12h for foals	Slow IV or IM
	75-100 mg	Subconjunctival
	125-250 mg	Intraarticular
	2 g buffered with equal volume of 75% sodium bicarbonate	Intrauterine
	15 mg/ml; combine 250 mg amikacin with 15 ml artificial tears	Ophthalmic
Aminocaproic acid	20 mg/kg diluted 1:9 in saline and administered over 30-60 min	IV
Aminophylline	5-10 mg/kg q12h	PO
Aminopropazine fumarate	0.5 mg/kg q12h	IM or IV

Continued

Name of Drug	Dose	Route
Aminopyrine	2.5-10 mg/450 kg	IV or IM
Ammonium chloride	20-520 mg/kg q24h (acidifier)	PO
Amoxicillin	10-22 mg/kg q8h	IM
trihydrate	6-10 mg/kg q12h-q8h	IM
Amphotericin B	0.05 mg/kg q2d for 1 month	IV
	Introduce over 5 days; dissolve in 1 L 5% dextrose and administer over 1 hour via large-bore catheter	
	0.15% solution in 5% glucose topically 4-6 times daily	Ophthalmic
Ampicillin Na	10-15 mg/kg q8h-q6h	IV or IM
trihydrate	11-22 mg/kg q12h or q8h	IM or PO
	50 mg	Subconjunctival
	50 mg/ml; reconstitute 1 g with 5 ml water and add 15 ml artificial tears	Ophthalmic
Antidiuretic hormone	60 IU q6h for diabetes insipidus	IV
Ascorbic acid	30 mg/kg q12h in IV fluids	IV
Aspirin	10-100 mg/kg q12h	PO
Atipamezole	0.05-1.0 mg/kg	IV
Atracurium	0.04-0.07 mg/kg	IV
Atropine	0.01-0.1 mg/kg	IV, IM, or SQ
Atropine HCl	0.5%-1.0% q6-48h	Ophthalmic
Aurothiogluconate	1 mg/kg	IM
Azathioprine	2-5 mg/kg q24h loading dose, then q48h for maintenance	PO
Azithromycin	10 mg/kg q24h for 5 days followed by q48h	PO
Azlocillin	25-75 mg/kg q6h	IV
Beclamethasone	3.75 mg q12h	Inhalation
Benztropine mesylate	8 mg	Slow IV drip
Betamethasone	0.02-0.1 mg/kg	IM or PO
	4-10 mg	Intralesional
Bethanecol	0.025-0.1 mg/kg q8h or q6h	SQ
	0.3-0.4 mg/kg q8h or q6h	PO
Bismuth subsalicylate	0.5-1 ml/kg q4-6h in foals	PO
	1-2 L/450 kg q12h	PO
Boldenone undecylenate	1 mg/kg repeated at 3-week intervals	IM
Botulinum antitoxin	100-150 IU/ml: 200 ml/foal or 500 ml/adult	IV or IM
Bretylium tosylate	3-10 mg/kg	IV
Buparavaquone	4-6 mg/kg, single dose	IV
Butorphanol tartrate	0.01-2 mg/kg, see xylazine, detomidine, and acepromazine	IV or IM
Caffeine	10 mg/kg loading dose, then 2.5-3 mg/kg q24h	PO
Calcium chloride	1-2 g/450 kg, slowly to effect	IV
Calcium gluconate	0.5 ml/kg of 10% solution	Slow IV
Cambendazole	20 mg/kg for <i>Strongyloides westeri</i>	PO
Captan	3% solution	Topical
Carbenicillin Na indanyl	50-80 mg/kg q12h or q8h	IV or IM
	200 mg	Subconjunctival
	6 g	Intrauterine
Carbon disulfide	24 mg/450 kg	PO
Carprofen	0.7 mg/kg q24h	IV
Casein (iodinated)	5 g q24h	PO
Cefaclor	20-40 mg/kg q8h	PO
Cefadroxil	22 mg/kg q12h	PO
	25 mg/kg q4-6h for foals	IV
Cefamandole	10-30 mg/kg q4-8h	IV or IM
Cefazolin Na	15 mg/kg q12h or q8h	IV or IM
	50 mg	Subconjunctival
	50 mg/ml; reconstitute 1 gm with 5 ml water and add 15 ml artificial tears	Ophthalmic

Name of Drug	Dose	Route
Cefepime	6 mg/kg q8h for adults 11 mg/kg q8h for foals	IV IV
Cefixime	400 mg/kg q8h	PO
Cefonicid	10-15 mg/kg q24h	IV or IM
Cefoperazone	30-50 mg/kg q12h or q8h	IV or IM
Ceforanide	5-10 mg/kg q12h	IV or IM
Cefotaxime Na	15-25 mg/kg q12h-q8h	IV or IM
Cefotetan	15-30 mg/kg q12h	IV or IM
Cefoxitin	30-40 mg/kg q8h or q6h 20 mg/kg q6h	IM IV
Ceftazidime	25-50 mg/kg q12h	IV or IM
Ceftiofur	1-5 mg/kg q24h-q12h 1 g	IV or IM Intrauterine
Ceftizoxime	25-50 mg/kg q12h or q8h	IV or IM
Ceftriaxone	25-50 mg/kg q12h	IV or IM
Cefuroxime axetil	25-50 mg/kg q8h 250-500 mg/kg q12h	IV or IM PO
Cephalexin	10-30 mg/kg q8h-q6h	PO
Cephalothin Na	20-40 mg/kg q8h-q6h 100 mg 50 mg/ml; reconstitute 1 gm with 5 ml water and add 15 ml artificial tears	IV or IM Subconjunctival Ophthalmic
Cephapirin	30 mg/kg q4-6h	IV or IM
Cetizoxime Na	20-30 mg/kg q8h	IV
Charcoal (activated)	1-3 g/kg as slurry (1 g in 5 ml water); repeat if necessary in 8-12 hours	PO
Chloral hydrate	60-200 mg/kg for foal restraint 40-100 mg/kg	IV PO
Chloramphenicol palmitate	4-10 mg/kg q8h or q6h (foal) 25-50 mg/kg q8h or q6h (adult)	PO PO
succinate	25 mg/kg q8h-q6h 50-100 mg	IV or IM Subconjunctival
Chlorhexidine	0.5%-2%	Topical
Chlorpromazine	1 mg/kg	IM
Cimetidine	6.6 mg/kg q4-6h 18 mg/kg q8h 2.5-4 mg/kg q8h for 2 months for tumor reduction	IV PO PO
Cisapride	0.1 mg/kg 0.5-0.8 mg/kg q8h for 7 days	IM PO
Clarithromycin	7.5 mg/kg q12h	PO
Clenbuterol	0.8-3.2 µg/kg q12h 0.8 µg/kg q12h 200 µg for uterine relaxation	PO IV IM or slow IV
Cloprostenol Na	250-500 µg/450 kg; can repeat in 30 min to 2 hours for parturition induction	IM
Clotrimazole	500 mg suspension or cream q24h for 1 week	Intrauterine
Cloxacillin	10-30 mg/kg q6h	IM
Cocaine chloride	1-1.5 ml of 10 mg/ml	Subconjunctival
Colistin	2500 IU/kg q6h	Slow IV
Corticotropin	1 IU/kg	IM
Coumaphos	0.06% wash, 0.1% dust	Topical
Cromolyn sodium	80-300 mg	Inhalation
Cyclophosphamide	200-300 mg/m ² q2-3wk	IV
Cyclosporin A	0.2%-2.0% topical q6-12h	Ophthalmic
Cyproheptadine	0.5 mg/kg q12h	PO
Cytosine arabinoside	200-300 mg/m ² q1-2 wk with chlorambucil or cyclophosphamide	IM or SQ
D-penicillamine	3-4 mg/kg q6h for 10 days	PO
Danthron	15-30 ml/kg	PO

Continued

Name of Drug	Dose	Route
Dantrolene Na	10 mg/kg loading dose; then 2.5 mg/kg q2h, maintenance	PO
	2-2.5 mg/kg in saline for acute myopathy	Slow IV
	1-2 mg/kg q24h to prevent myositis	PO
Dembrexine	0.3-0.5 mg/kg	PO
Demecarium bromide	0.25% q12h	Ophthalmic
Detomidine	0.005-0.02 mg/kg	IV
	0.01-0.02 mg/kg followed by 0.044-0.066 mg/kg butorphanol	IV
	0.02-0.04 mg/kg followed by 2.2 mg/kg ketamine	IV
Dexamethasone	0.02-0.2 mg/kg q24h	IV, IM, or PO
	0.5-2 mg/kg for septic shock	IV
	100 mg/450 kg q24h for 5 days to induce parturition	IV
phosphate	0.1% q8h	Ophthalmic
suspension	0.1% q3-8h	Ophthalmic
Dextran (6% solution)	8 g/kg q24h for up to 3 days	IV
Diazepam	0.03-0.5 mg/kg; repeat in 30 minutes if necessary	Slow IV
Dichlorphenamide	1 mg/kg q12h	PO
Dichlorvos	35 mg/kg	PO
	0.93% solution	Topical
Dicloxacillin	10 mg/kg q6h	IM
Diethylcarbamazine	1 mg/kg q24h for 21 days for onchocerciasis	PO
	50 mg/kg q24h for 10 days for verminous myelitis	PO
Digoxin	0.002 mg/kg q12h	IV
	0.01 mg/kg q12h	PO
Dihydrostreptomycin	11 mg/kg q12h	IM or SQ
Dimercaprol	2.5-5 mg/kg as 10% solution in oil q4h for 2 days, then q12h until recovery	IM
Dimethyl glycine	1-1.6 mg/kg q24h	PO
Dimethyl sulfoxide (DMSO)	0.5 mg/kg to 1.0 g/kg (10% solution in 5% dextrose); repeat lower doses q6-12h	IV
	50% solution	Topical
Dinoprost tromethamine	10 mg/450 kg	IM
Dioctyl sodium sulfosuccinate	10-20 mg/kg in 4-8 L water q48h	PO
5% solution	10 ml in warm water as enema for retained meconium	
Dioxathion	0.15% wash	Topical
Diphenylhydantoin	1-10 mg/kg q2-4h	IV, IM, or PO
Dipyrone	5-22 mg/kg	IV or IM
Dobutamine	1-10 µg/kg per minute (250 mg in 500 ml saline infused at 0.45 ml/kg per hour)	IV
Dolophine HCl	0.2-0.4 mg/kg	IM
Domperidone	0.2 mg/kg	IV
	1.1 mg/kg q24h	PO
Dopamine	1-5 µg/kg per minute (200 mg in 500 ml saline infused at 0.45 ml/kg per hour)	IV
Doxapram	0.5-1.0 mg/kg q5min (do not exceed 2 mg/kg in foals)	IV
	0.02-0.05 mg/kg per minute up to 400 mg total for neonatal foal resuscitation	IV
Doxepin hydrochloride	0.5-0.75 mg/kg q12h	PO
Doxycycline	3 mg/kg q12h	PO
	0.3% topically q3-6h	Ophthalmic
Ecothiophate iodide	0.03% q12h	Ophthalmic
EDTA calcium disodium	75 mg/kg per day in divided doses for lead poisoning	Slow IV
	6.6% solution (1 ml/0.9 kg), q8-12h	IV
Eltenac	0.5 mg/kg	IV
Enalapril	0.5 mg/kg q12-24h	PO
Enrofloxacin	2.5 mg/kg q12h	PO
Ephedrine sulphate	0.7 mg/kg q12h	PO
Epinephrine	1-1.5 ml of 0.33 ng/ml	Subconjunctival
	0.01-0.02 mg/foal (foal resuscitation)	IV
	0.1-0.2 mg/foal (foal resuscitation)	Intratracheal

Name of Drug	Dose	Route
Erythromycin base	0.1 mg/kg per hour to enhance gut motility	IV
estolate or ethylsuccinate	25 mg/kg q12h	PO
lactobionate	2.5-5 mg/kg q8h or q6h	IV
phosphate or stearate	20-40 mg	Subconjunctival
Estradiol	37.5 mg/kg q12h	PO
Estrone sulfate	0.004-0.008 mg/kg q2d for urinary incontinence	IM
Ethyl alcohol (50%)	0.04 mg/kg q24h	IM
Ethylene diamine dihydriodide	5-10 ml/50 kg	Aerosol
Ethylenediaminetetraacetic acid (EDTA)	0.5-1.5 g/450 kg q24h	PO
Etodolac	0.5% topical solution q2-4h	Ophthalmic
Famotidine	10-15 mg/kg q24h	IV or PO
Febantel	3.3 mg/kg q8h	PO
Fenbendazole	6 mg/kg	PO
	5 mg/kg	PO
	10 mg/kg for <i>Parascaris equorum</i>	PO
	50 mg/kg q24h for 3 days for verminous arteritis	PO
	50 mg/kg for <i>Strongyloides westeri</i>	PO
	50 mg/kg q24h for 5 days for onchocerca	PO
Fenoterol	2-4 µg/kg	Inhalation
Fenoprostalene	0.5 mg/450 kg	SQ
Fentanyl	Two 10 mg patches	
Ferrous sulfate	2 mg/kg q24h	PO
Florfenicol	Do not administer to horses until more data are available	
Floxacin	10 mg/kg q6h	IM
Fluconazole	4 mg/kg q24h	PO
Flumazenil	0.5-2.0 mg	Slow IV
Flumethasone	0.002-0.008 mg/kg	PO
Flunixin meglumine	0.25-1.1 mg/kg q24h-q8h	PO, IM, or IV
Fluoroprednisolone acetate	5-20 mg/450 kg	IM
Fluphenazine	25 mg/pony (at 320 days gestation for prevention of fescue toxicosis)	IM
Fluprostenol	250 µg/450 kg	IM
Flurbiprofen Na 0.03%	q8h or q6h	Ophthalmic
Fluticasone propionate	2000 µg/450 kg	Inhalation
Folic acid	40-75 mg	IM
Folinic acid	50-100 mg	IM
Follicle stimulating hormone	10-50 mg/450 kg	IV, IM, or SQ
Furazolidone	4 mg/kg q8h	PO
Furosemide	1-3 mg/kg q12h	IV or IM
	250-500 mg 1-4 hours prerace	IV or IM
Gentamicin sulfate	2-4 mg/kg q12h-q6h	IV, IM, or SQ
	6.6-8.8 mg/kg q24h	IV, IM, or SQ
	10-40 mg	Subconjunctival
	150 mg (unbuffered)	Intraarticular
	1-2 g buffered in equal volume of 75% sodium bicarbonate	Intrauterine
	6 mg/ml; combine 100 mg with 15 ml artificial tears	Ophthalmic
Glucagon	25-50 mg/kg	IV
Glycerin	1 g/kg	PO
Glycerol	0.5-2 g/kg for brain edema	IV
Glycerol (5%)	2-5 ml/50 kg	Aerosol
Glycerol guaiacolate	110 mg/kg for convulsions	IV
	0.1-0.2 g/50 kg q6h expectorant	PO
Glycopyrolate	0.005-0.01 mg/kg	IV
Glycosaminoglycan polysulfated	250 mg once weekly	Intraarticular
	1 mg/kg q5days	IM
Gonadotropin-releasing hormone	0.05 mg 2 and 0.5 hours prebreeding for low libido	SQ
	0.04 mg 6 hours prebreeding to induce ovulation	IM
Griseofulvin	10 g/450 kg q24h for 2 weeks, then 5 g q24h for 7 weeks	PO
Guaifenesin (5%-10%)	To effect (~50-110 mg/kg needed for induction)	Slow IV
	5% with 4.4 mg/kg thiamylal	Rapid IV

Continued

Name of Drug	Dose	Route
Heparin	10 IU/kg loading dose 15 IU/kg per hour maintenance 40-100 IU/kg q12h or q6h for acute laminitis	IV Slow IV IV
Heparin calcium	20-90 IU/kg for peritonitis prevention 150 IU/kg loading dose, then 125 IU/kg q12h for 6 doses, then 100 IU/kg	SQ SQ
Heparin sodium	40-80 IU/kg 2 hours later, 40 IU/kg, then 40 IU/kg q12h	IV SQ
Heparin (low-molecular-weight)	50 IU/kg q12h	SQ
Hetastarch	5-10 ml/kg/day	IV
Human chorionic gonadotrophin	2000 IU to synchronize ovulation	IV
Hyaluronate Na	10-50 mg/joint (see manufacturer's recommendations) 500 mg q4d for 7 doses	Intraarticular IM
Hyaluronic acid	20-120 mg locally around inflamed tendon 20-50 mg	Intraarticular IV
Hydralazine	0.5 mg/kg	IV
Hydrochlorothiazide	250 mg/450 kg q24h	PO
Hydrocortisone sodium succinate	1-4 mg/kg	IV drip
Hydroxyethyl starch	See <i>Hetastarch</i>	
Hydroxyzine HCl	0.5-1 mg/kg q12h	IM or PO
Hyoscine	0.14 mg/kg	IV
Idoxuridine 0.1%	q2-6h	Ophthalmic
Imidocarb dipropionate	2 mg/kg q24h for 2 days for <i>Babesia caballi</i> 4 mg/kg q3d for 4 treatments for <i>Babesia equi</i>	IM IM
Imipenem	15 mg/kg q6-8h for foals	IV
Imipramine	100-600 mg q12h for 2 weeks to improve ejaculation 0.55 mg/kg q8h 1.5 mg/kg q8h	PO IM or IV PO
Insulin	0.5 IU/kg	IM or SQ
Insulin—protamine zinc	0.15 IU/kg q12h	IM or SQ
Interferon- α 2A (1,000 IU/ml)	1 ml q24h for 3 weeks, one week off, then repeat	PO
Iodide Na	20-40 mg/kg q24h for several weeks	PO
Iodochlorhydroxyquin	10 g/450 kg (repeat for 3-4 days then gradually reduce dose if response is obtained)	PO
Ipratropium	2-3 μ g/kg	Inhalation
Iron cacodylate	1 g	IV
Isoflupredone acetate	10-14 mg	IM
Isoniazid	5-20 mg/kg q24h	PO
Isoproterenol HCl	0.4 μ g/kg by slow infusion (discontinue when heart rate doubles) 0.05-1 μ g/kg per minute for foal resuscitation	IV IV
Isoproterenol (0.05%)	5-10 ml/50 kg q6h	Aerosol
Isoxsuprine HCl	0.4-1.2 mg/kg q12h	IM
Itraconazole	3 mg/kg q12h for up to 2 months 1% with 30% DMSO topically q4-6h (not for use with subpalpebral lavage system)	PO Ophthalmic
Ivermectin	0.2 mg/kg 0.2 mg/kg twice at 4-day intervals for lice and mange	PO PO
Kanamycin	7.5 mg/kg q8h 1-2 g	IV or IM Intrauterine
Kaopectate	2-4 qt/450 kg q12h	PO
Ketamine	See xylazine and detomidine	
Ketoconazole	30 mg/kg q24h or q12h (dissolve in 0.2 N HCl)	PO
Ketoprofen	2.2 mg/kg	IV or IM
L-asparaginase	10,000-40,000 IU/m ² q2-3wk	IM
Lactase	6,000-9,000 FCC units q3-6h	PO
Lactulose	0.2 ml/kg q12h	PO
Levallorphan tartrate	0.02-0.04 mg/kg	IV
Levamisole	8-11 mg/kg q24h	PO
Levothyroxine	10 mg in 70 ml Karo syrup q24h	PO

Name of Drug	Dose	Route
Lidocaine	0.2-0.5 mg/kg bolus q5min up to 1.5 mg/kg total dose	IV
	1.3 mg/kg bolus over 5 minutes, then 0.05 mg/kg per minute for up to 24 hours for treatment of ileus	IV
	1-2 mg/kg followed by 20-50 µg/kg/min for ventricular arrhythmias in foals	IV
Lime sulfur	3%-5%	Topical
Lindane	3% spray	Topical
Loperamide	0.1-0.2 mg/kg q6h	PO
Magnesium hydroxide	200-250 ml q8h (antacid)	PO
Magnesium sulfate	0.2-1 g/kg dissolved in 4 L warm water q24h	PO
	4 mg/kg boluses q2min up to 50 mg/kg total dose	IV
Malathion	0.5% wash, 5% dust	Topical
Mannitol (20%)	0.25-2.0 g/kg	Slow IV
Mebendazole	8.8 mg/kg	PO
	20 mg/kg q24h for 5 days for <i>Dictyocaulus arnfieldi</i>	PO
	50 mg/kg q24h for 5 days for onchocerciasis	PO
Meclofenamic acid	2.2 mg/kg q12h	PO
Megestrol acetate	65-85 mg/kg q24h	PO
Meperidine	See acepromazine	
Metaclopramide HCl	10 mg/kg	IV
Methadone	0.05-0.2 mg/kg	IV
Methetharimide	10-20 mg/kg	IV
Methicillin	25 mg/kg q4-6h	IM
	100 mg	Subconjunctival
Methionine (D-L)	1 g/kg q24h	PO
Methocarbamol	5-55 mg/kg q6h	Slow IV
	40-300 mg/kg for convulsions	Slow IV
Methoxychlor	0.5% wash	Topical
Methylcellulose flakes	0.25-0.5 kg/450 kg in 10 L water	PO
Methylene blue	8.8 mg/kg as 1% solution	IV
Methylprednisolone acetate	0.2-0.7 mg/kg	IM
sodium succinate	2-4 mg/kg	IV
	30 mg/kg, then 5.4 mg/kg per hour for 23 hours for CNS trauma	IV
	20 mg	Subconjunctival
	Up to 100 mg	Intrabursal or intraarticular
Methylsulfonylmethane	30 g/450 kg q24h	PO
Methysulfmethoxine	15-20 mg/kg q24h	PO
Metoclopramide	0.25 mg/kg q8h or q6h	IV drip or SQ
	0.6 mg/kg q4h	PO
Metronidazole	15 mg/kg q6h	IV or PO
Mezlocillin	25-75 mg/kg q6h	IV
Miconazole	2% vaginal cream topically q4-6h (not for use with subpalpebral lavage system)	Ophthalmic
	1% solution used topically q4-6h	Ophthalmic
Midazolam	0.05-0.2 mg/kg	IV or IM
Mineral oil	10 ml/kg q24h	PO
Minocycline	3 mg/kg q12h	PO
Misoprostol	1-4 µg/kg q24h	PO
Morphine sulfate	0.2-0.4 mg/kg	IM
	0.25-0.75 mg/kg	IV
Moxalactam	50 mg/kg q8h	IV or IM
Moxidectin	0.4 mg/kg	PO
Nafcillin	10 mg/kg q6h	IM
Naloxone	0.01-0.02 mg/kg	IV
Naproxen	10 mg/kg q24h or q12h	PO or IV
Natamycin	Topically q4-6h; dilute to 3.33% for use with subpalpebral lavage system	Ophthalmic

Continued

Name of Drug	Dose	Route
Neomycin	1 g/horse q6h 2 g/horse q12h 0.5 g/foal q6h 1.5 g/foal q12h 3-4 g 5 mg/kg q8h for 2 days to reduce ammonia production in the bowel	PO PO PO PO Intrauterine PO
Neostigmine	0.004-0.02 mg/kg	SQ
Netilmicin	2 mg/kg q12h-q8h	IV or IM
Niclosamide	100 mg/kg	PO
Nitrofurantoin	3 mg/kg q12h	IM
Nizatidine	6.6 mg/kg q8h	PO
Norepinephrine	0.01 mg/kg	IM
Nystatin	500,000 IU in 30 ml saline q24h for 7-10 days	Intrauterine
Omeprazole	1.5 mg/kg q24h	IV
Ouabain	2.5-3 mg/450 kg q2h until heart rate slows or intoxication develops; do not exceed 10 g total	IV
Orbifloxacin	2.5 mg/kg q24h	PO
Oxacillin	25-50 mg/kg q12h or q8h	IV or IM
Oxfendazole	10 mg/kg	PO
Oxibendazole	10-15 mg/kg 15 mg/kg for <i>Strongyloides westeri</i>	PO PO
Oxymorphone	0.02-0.03 mg/kg	IM
Oxytetracycline	5-20 mg/kg q24h 44-70 mg/kg (single dose for tendon contracture in foals)	IV IV
Oxytocin	2.5-5 IU/450 kg as bolus q20min 80-100 IU in 500 ml saline 10-20 IU/450 kg 1-3 IU/450 kg for milk letdown 0.5-10 IU/kg to induce parturition	IV Slow IV IM or IV IV IV
Pancuronium	0.04-0.066 mg/kg	IV
Paromomycin	100 mg/kg q24h	PO
Penicillamine D	3-4 mg/kg q6h for 10 days	PO
Penicillin G		
Na	10,000-50,000 IU/kg q6h	IV or IM
K	10,000-50,000 IU/kg q6h	IV or IM
	20,000 IU/kg q6h	PO
	5×10^6 IU	Intrauterine
procaine	20-50,000 IU/kg q12h or q8h	IM
benzathine	10,000-40,000 IU/kg q48-72h	IM
Penicillin V	110,000 mg/kg q12h-q6h	PO
Pentazocine	0.8 mg/kg	IV
Pentobarbital	2-20 mg/kg for convulsions	IV
Pentosan sulfate	250 mg q7-10d	Intraarticular
Pentoxifylline	8.4 mg/kg q12h	PO
Pentyleneetetrazol	6-10 mg/kg	IV
Pergolide mesylate	"High dose" 0.006-0.01 mg/kg q24h "Low dose" 0.002 mg/kg q24h	PO PO
Permethrin	2%	Topical spray
Perphenazine	0.3-0.5 mg/kg q12h	PO
Phenobarbital	5-25 mg/kg in 30 ml saline for convulsing foals	IV over 30 minutes
	9 mg/kg q8h for maintenance	IV
Phenothiazine	55 mg/kg 27.5 mg/kg with piperazine	PO PO
Phenoxybenzamine HCl	0.7-1 mg/kg in 500 ml saline q8h or q6h	IV
Phenylbutazone	2-4.4 mg/kg q12h	PO or IV
Phenylephrine	10%	Ophthalmic
	0.1-0.2 µg/kg/min; total dose not to exceed 0.01 mg/kg	IV
Phenytoin	5-10 mg/kg for convulsing foals 1-5 mg/kg for maintenance q4h 10-22 mg/kg q12h for digoxin-induced arrhythmias	IV IV, IM, or PO PO

Name of Drug	Dose	Route
Physostigmine	0.1-0.6 mg/kg	IM or slow IV
Pilocarpine HCl	4% gel q12h-q6h	Ophthalmic
Piperazine	88-110 mg/kg	PO
Piperacillin	15-50 mg/kg q12h-q6h	IV or IM
Pirbuterol	1-2 µg/kg	Inhalation
Polymixin B or E	5000-10,000 IU/kg q6h	PO
	1 × 10 ⁶ IU	Intrauterine
Ponazuril	5 mg/kg q24h for 28 days	PO
Potassium chloride	40 g in 4-6 L water q12h	PO
	20-40 mEq/L of fluid	IV
Potassium iodide	2-20 g q24h	PO
Potassium permanganate	1% solution for mouthwash	
Povidone iodine	5% solution topically q24h (irritating to conjunctiva)	Ophthalmic
Pralidoxime chloride	20-50 mg/kg	Slow IV or IM
Praziquantel	0.5-1.0 mg/kg for tapeworms	PO
Prednisolone acetate	1% topical q1-6h	Ophthalmic
Prednisolone	0.2-4.4 mg/kg q24h or q12h	PO or IM
Na succinate	2-5 mg/kg for septic shock	IV
Primidone	1-2 g/foal q12h-q6h	PO
Procainamide	35 mg/kg	PO
Progesterone	150 mg q24h to suppress estrus	IM
	300 mg q24h to maintain pregnancy	IM
repositol	1000 mg/450 kg once weekly for abortion prevention	IM
Promazine	0.25-1 mg/kg	IV
	1-2 mg/kg granules	PO
Propafenone	0.5-1.0 mg/kg	IV
Propantheline bromide	0.014 mg/kg	IV
Proparacaine	0.5%	Ophthalmic
Propofol	2.4 mg/kg for anesthesia induction in foals, then 0.3 mg/kg per minute for maintenance	IV
Propranolol	0.38-0.78 mg/kg q8h	PO
	0.05-0.16 mg/kg q12h	IV
Prostaglandin-E ₂ analogues	1-4 µg/kg q24h for gastric protection	PO
Prostaglandin F _{2α}	10 mg	IM
Prostalene	2 mg/450 kg, 2 doses 2 weeks apart	SQ
Psyllium mucilloid	1 g/kg q24h-q6h	PO
Pyrantel embonate	38 mg/kg for tapeworms	PO
tartrate	2.64 mg/kg q24h for control of intestinal nematodes	PO
pamoate	6.6 mg/kg	PO
	13.2 mg/kg for tapeworms	PO
Pyrimethamine	1 mg/kg	IV, IM, or SQ
	0.25 mg/kg q12h for 3 days then q24h for 27 days (for equine protozoal myeloencephalitis)	PO
Quinidine sulfate	22 mg/kg q2-6h	PO
gluconate	2.2 mg/kg q10min until 8-10 mg/kg total	IV
	0.7-3 mg/kg per hour	IV
Ranitidine	6.6 mg/kg q8h	PO
	1.5 mg/kg q8h	IV
Reserpine	2-5 mg/kg q24h	PO
Rifampin	10-20 mg/kg q24h	PO
	3-5 mg/kg q12h with erythromycin for <i>Rhodococcus equi</i>	PO
Romifidine	0.08-1.0 mg/kg	IV
Ronnel	2.5% spray	Topical
Saline (hypertonic)	7.5%, 4 ml/kg for hypovolemia	IV over 20 minutes
Selenium (Na selenite)	5.5 mg/450 kg	IM
Silver sulfadiazine	1% cream topically q4-6h (not for use with subpalpebral lavage system)	Ophthalmic
Sodium bicarbonate	30-150 g/day	PO
Sodium hypochlorite	0.5%	Topical
Sodium iodide	20-40 mg/kg q24h	PO

Continued

Name of Drug	Dose	Route
Sodium sulfate	Up to 3 g/kg dissolved in warm water	PO
Sodium thiosulfate (20%)	0.22 ml/kg	Slow IV
Spectinomycin	20 mg/kg q8h	IM
Stanozolol	0.5 mg/kg, up to 4 doses q1-2 wk	IM
Stilbestrol	30 mg/450 kg	IM
Stirofos	1% wash	Topical
Streptomycin	11 mg/kg q12h	IM or SQ
Succinylcholine	330 mg/kg	IV or IM
Sucralfate	1-4 g q12h-q6h	PO
Sulfonamides	100-200 mg/kg on day 1, then 50-100 mg/kg subsequently (check labels on each product)	IV, IM, or SQ
Sulfonamides, potentiated	30 mg/kg q12h or q8h	PO
Sulpiride	3.3 mg/kg q24h	PO
Suprofen 1%	q12h-q8h	Ophthalmic
Telazol	1-2 mg/kg for anesthesia induction	IV
Terbutaline	0.02-0.06 mg/kg q12h	IV, PO, or inhalation
Testosterone (aqueous)	0.1-0.2 mg/kg q48h for 2 weeks for inadequate libido	SQ
Tetanus antitoxin	100 IU/kg q3-5days for treatment of tetanus	IM, SQ, or IV
Tetracycline	6.6-11 mg/kg q12h	IV
Tetramethrin	0.4% solution, wipe-on	Topical
Theophylline	1 mg/kg q6h	PO
Thiabendazole	44 mg/kg 88 mg/kg for <i>Parascaris equorum</i> 440 mg/kg q24h for 2 days for verminous arteritis 4% solution in saline or 90% DMSO	PO PO PO Topical
Thiamine HCl	0.5-5 mg/kg	IM
Thiamylal Na	2-4 mg/kg	IV
Thiopental	4-10 mg/kg as 10% solution	IV
Thyroxine L	0.01 mg/kg q24h	PO
Ticarcillin	40-80 mg/kg q8h	IV or IM
clavulanate	6 g 50 mg/kg q8h-q6h	Intrauterine IV
Ticarcillin/clavulanic acid	6 g/200 mg	Intrauterine
Tilmicosin	Do not administer to horses until more data are available.	
Timolol maleate	0.5% q12h	Ophthalmic
Tobramycin	1-1.7 mg/kg q8h (human dose) 10-30 mg 6 mg/ml; combine 100 mg with 15 ml artificial tears	IV or IM Subconjunctival Ophthalmic
Tocopherol acetate	6000 IU/250-500 kg q24h	PO

Name of Drug	Dose	Route
Tolazoline	0.5 mg/kg	IV
Toxaphene	0.5% wash	Topical
Tranexamic acid	1 g	IV
Triamcinolone	0.02-0.1 mg/kg	IM
	1-3 mg/site up to 18 mg total	Intralesional
	1-2 mg	Subconjunctival
Trichlorfon	40 mg/kg	PO
Trichlormethiazide	200 mg/450 kg	PO
Trifluorothymidine 1%	q1-2h	Ophthalmic
Triflupromazine	0.2-2.0 mg/kg	IV
Trifluridine 1%	q2-6h	Ophthalmic
Trimethoprim-sulfadiazine	15 mg/kg q12h	IV
	15-30 mg/kg q12h	PO
	2.5-5 g q24h	Intrauterine
Tripelennamine HCl	1 mg/kg	IV or IM
Tromethamine	300 mg/kg	IV
Tropicamide	0.5%-1%	Ophthalmic
Tylosin	10 mg/kg q12h	IM
Vancomycin	20-40 mg/kg q12h-q6h	IV or PO
Vedaprofen	2.2 mg/kg q12h	IV
Verapamil	0.025-0.5 mg/kg q30min	IV
Vidarabine	3% ointment at least q6h	Ophthalmic
Vincristine	0.01-0.025 mg/kg q7d	IV
Vinegar	250 ml/450 kg q24h for enterolith prevention	PO
Vitamin B complex	20-30 ml q24h	PO
Vitamin C	See <i>Ascorbic acid</i>	
Vitamin E	1500-2000 IU q24h for equine degenerative myeloencephalopathy prophylaxis	PO
	6000-9000 IU q24h for treatment of equine degenerative myeloencephalopathy	PO
Vitamin K ₁	0.5-1 mg/kg q4-6h for warfarin toxicosis	SQ
	1-2 mg/kg (divided at several sites) for sweet clover poisoning	SQ
	0.5-2 mg/kg for foals	IM
Voltaren	Topical q1-6h	Ophthalmic
Xylazine	0.2-1.1 mg/kg	IV
	0.33-0.44 mg/kg followed by 0.033-0.066 mg/kg butorphanol	IV
	1.1 mg/kg followed by 1.75-2.2 mg/kg ketamine	IV
	0.6 mg/kg with 0.02 mg/kg acepromazine	IV
	0.66 mg/kg to ejaculate ex-copula	IV
Yohimbine	0.12 mg/kg for xylazine or detomidine antagonism	Slow IV
	0.075 mg/kg to restore intestinal motility	IV

IM, Intramuscular; IV, intravenous; PO, by mouth; SQ, subcutaneous; q, every; h, hour; d, day; wk, week.

This table was composed from doses recommended by authors in this and previous editions of *Current Therapy in Equine Medicine*. It is recommended that the manufacturer's literature be checked before a drug is used. Many drugs have not been approved for use in horses.

APPENDIX 2

Normal Clinical Pathology Data

BRUCE W. PARRY
Werribee, Australia

Evaluation of laboratory tests is a useful adjunct to a carefully collected history and physical examination in many clinical cases. The following laboratory data are derived from the veterinary literature. Clinicians must be aware that these reference values may not be directly applicable to their laboratory data. Differences in reference ("normal") values may arise because of differences in the population of animals studied (e.g., geographic location, physical activity, age, breed, sex, etc.), and the methodology of the test (e.g., reagents, reaction temperatures, equipment, etc.). Nevertheless, the following data provide a guide to results expected in a population of "normal" animals.

HEMATOLOGY

Horses are usually grouped as hot-blooded or cold-blooded. The former are basically those of Arabian ancestry and include Arabians, Quarter Horses, Standardbreds, and Thoroughbreds. Cold-blooded horses are basically draught-type animals, including Clydesdales, Percherons, and Shires. The latter group has somewhat lower reference limits for erythrocyte (RBC) parameters but similar leukocyte (WBC) data. Warm-blooded horses, such as Hanoverians and Trakehners, and ponies are more similar to hot-blooded than cold-blooded horses in their hematology.

Important points to remember about equine hematology are as follows:

1. The equine spleen is a very dynamic organ.
Excitement and exercise readily cause splenic

contraction and a "relative" (physiological) polycythemia. In contrast various tranquilizers, such as acepromazine and xylazine, cause splenic relaxation and an apparent anemia.

2. Foals (younger than about 9 months) tend to have lower packed cell volume (PCV) and mean corpuscular volume (MCV) values than adults. However, their mean corpuscular hemoglobin concentration (MCHC) is comparable.
3. From a practical viewpoint, the following are true:
 - a. Males and females have virtually the same RBC and WBC parameters.
 - b. Hemoglobin concentration, PCV, and RBC count tend to increase during pregnancy.
 - c. Seasonal differences, although reported, are not routinely considered in hematologic evaluations.
4. Horses do not release reticulocytes into the circulation under resting conditions or in response to an anemia. Numbers of reticulocytes will increase in the bone marrow in the latter situation. Measuring PCV in a blood sample at 3- to 5-day intervals most readily assesses the response of the bone marrow to anemia. Provided that the rate of RBC production exceeds the rate of loss or destruction, PCV will increase. If this is not occurring, assessment of RBC histograms may be useful. Younger (less mature) RBCs are slightly larger than their mature counterparts. Although this may not increase the MCV of a blood sample, it may increase the proportion of larger cells and thereby the index of anisocytosis (IA) in a RBC histogram.

Please see bibliography at the end of this appendix for citations of works cited throughout.

Hematology: Adult Hot-Blooded Horses

		LUMSDEN AND COLLEAGUES (1980)*		JAIN (1986)†
		Thoroughbred Mares (n = 59-60)	Standardbreds (n = 49-50)	Hot-Blooded Horses (n = 147)
Hemoglobin (Hb)	g/dl	10.9-18.8	11.3-17.9	11.0-19.0
	g/L	109-188	113-179	110-190
Packed cell volume (PCV)	%	29-53	31-48	32-53
	L/L	0.29-0.53	0.31-0.48	0.32-0.53
Red cell count (RCC)	$\times 10^6/\mu\text{l}$	6.5-11.6	6.9-10.7	6.8-12.9
	$\times 10^{12}/\text{L}$	6.5-11.6	6.9-10.7	6.8-12.9

* Lumsden and colleagues (1980): All values 2.5 to 97.5 percentiles.

† Jain (1986): Ranges.

Hematology: Adult Hot-Blooded Horses—cont'd

		LUMSDEN AND COLLEAGUES (1980)*		JAIN (1986)†
		Thoroughbred Mares (n = 59-60)	Standardbreds (n = 49-50)	Hot-Blooded Horses (n = 147)
MCV	fL	39-49	40-49	37-59
MCHC	g/dl	34-39	35-41	31-39
	g/L	337-386	350-410	310-386
Leukocytes	/μl	5300-11,000	4900-10,000	5400-14,300
	×10 ⁹ /L	5.3-11.0	4.9-10.0	5.4-14.3
Band neutrophils	/μl	0-200	0-400	0-1,000
	×10 ⁹ /L	0-0.2	0-0.4	0-1.0
Segmented neutrophils	/μl	2100-6000	2000-5500	2260-8580
	×10 ⁹ /L	2.1-6.0	2.0-5.5	2.3-8.6
Lymphocytes	/μl	1700-5000	1600-4600	1500-7700
	×10 ⁹ /L	1.7-5.0	1.6-4.6	1.5-7.7
Monocytes	/μl	0-600	0-600	0-1,000
	×10 ⁹ /L	0-0.6	0-0.6	0-1.0
Eosinophils	/μl	0-800	0-700	0-1000
	×10 ⁹ /L	0-0.8	0-0.7	0-1.0
Basophils	/μl	0-100	0-100	0-290
	×10 ⁹ /L	0-0.1	0-0.1	0-0.3
Platelets	/μl	80,000-397,000	81,000-240,000	100,000-350,000
	×10 ⁹ /L	80-397	81-240	100-350
RBC IA‡	fl	16-24		
Refractometer protein	g/dl		5.4-7.5	
	g/L		54-75	
Fibrinogen	mg/dl		150-380	
	g/L		1.5-3.8	

MCV, Mean corpuscular volume; MCHC, mean corpuscular hemoglobin concentration.

*Lumsden and colleagues (1980): All values 2.5 to 97.5 percentiles.

†Jain (1986): Ranges.

‡Weiser (1982): RBC index of anisocytosis (IA), mean ± 2SD, n = 75.

Hematology: Hot-Blooded Foals

		AGE			
		1 Day	1 Week	1 Month	6 Months
Hb	g/dl	11.7-16.5	11.8-17.6	10.9-15.6	10.8-14.0
	g/L	117-165	118-176	109-156	108-140
PCV	%	34-46	31-44	28-42	31-41
	L/L	0.34-0.46	0.31-0.44	0.28-0.42	0.31-0.41
RCC	×10 ⁶ /μl	8.8-11.0	7.8-9.6	8.0-10.9	8.6-10.7
	×10 ¹² /L	8.8-11.0	7.8-9.6	8.0-10.9	8.5-10.7
MCV	fL	37-49	35-42	35-39	32-40
MCHC	g/dl	31-38	35-40	33-39	34-39
	g/L	310-380	350-400	330-390	340-390
Leukocytes	/μl	4500-11,500	7200-13,500	4600-12,900	7400-10,800
	×10 ⁹ /L	4.5-11.5	7.2-13.5	4.6-12.9	7.4-10.8
Segmented neutrophils	/μl	3040-9570	5020-10720	1720-9740	2890-5560
	×10 ⁹ /L	3.0-9.6	5.0-10.7	1.7-9.7	2.9-5.6
Lymphocytes	/μl	630-2060	1040-3800	1780-9740	3200-6910
	×10 ⁹ /L	0.6-2.1	1.0-3.8	1.8-9.7	3.2-6.9
Monocytes	/μl	50-380	20-430	50-710	40-590
	×10 ⁹ /L	0.05-0.4	0.02-0.4	0.05-0.7	0.04-0.6
Eosinophils	/μl	0-108	0-134	0-540	42-728
	×10 ⁹ /L	0-0.1	0-0.1	0-0.5	0.04-0.7

Harvey and colleagues (1984): ranges, n = 22.

Continued

Hematology: Hot-Blooded Foals—cont'd

		AGE			
		1 Day	1 Week	1 Month	6 Months
Basophils	/μl	0-35	0-238	0-129	0-74
	×10 ⁹ /L	0-0.04	0-0.2	0-0.1	0-0.07
Platelets	/μl	125,000-390,000	98,00-385,000	135,000-458,000	187,000-405,000
	×10 ⁹ /L	125-390	98-385	135-458	187-405
Refractometer protein	g/dl	5.1-7.7	5.1-7.5	5.6-7.8	6.2-7.0
	g/L	51-77	51-75	56-78	62-70
Fibrinogen	mg/dl	110-450	160-420	230-710	160-490
	g/L	1.1-4.5	1.6-4.2	2.3-7.1	1.6-4.9

Harvey and colleagues (1984): ranges, n = 22.

COAGULATION TESTS**Activated Partial Thromboplastin Time and Prothrombin Time**

Results for these tests may vary greatly depending on the methodology and reagents used. It is important that the laboratory performing the tests be familiar with results expected for equine specimens. Ideally an equine control pool specimen will be processed concurrently. Mixing equal volumes of citrate anticoagulated plasma from at least 8 clinically normal horses produces such a control plasma pool.

Activated partial thromboplastin time (APTT) has been reported as 47 to 73 seconds (Dorner and Bass, 1974) and 36 to 47 seconds (Meyers and colleagues, 1982).

Prothrombin time (PT) has been reported as 9.7 to 11.7 seconds (Dorner and Bass, 1974) and 8.0 to 12.4 seconds (Meyers and colleagues, 1982).

An alternative approach is to calculate the ratio of the patient and control pool values to attempt to standardize results. With such a method, reference APTT and PT values are reported as 0.75 to 1.25 (Johnstone and Crane, 1986). Values (ratios) greater than 1.25 are increased (prolonged).

A prolonged APTT with a normal PT suggests a deficiency of one (or more) of the factors in the intrinsic pathway, namely high molecular weight kininogen, pre-kallikrein, XII, XI, IX, or VIII. A prolonged PT with a normal APTT indicates a deficiency of factor VII (in the extrinsic pathway). A prolonged APTT and PT indicates a deficiency of one (or more) of the factors in the intrinsic and extrinsic pathways or in the common pathway. The latter is most likely to be an acquired disorder with several factors decreased in concentration. It may be associated with anticoagulant administration (e.g., heparin) or poisoning (e.g., vitamin K antagonists) or with disseminated intravascular coagulation (DIC).

Antithrombin III

Antithrombin III (ATIII) activity may decrease in animals with a protein-losing glomerulopathy or those in DIC. It has been advocated as a prognostic guide in colic cases. Reference values for ATIII are 75% to 126% (Stephens and colleagues, 1984).

Fibrin Degradation Products

Fibrin degradation products (FDP) concentration increases in cases with DIC. It has been advocated as a prognostic guide in colic cases. Reference values for FDP are less than 10 μg/ml (Meyers and colleagues, 1982) and less than 20 μg/ml (Johnstone and Crane 1986).

Specific Factors

Assessment of specific clotting factors is warranted if a congenital coagulopathy is suspected. As a generalization, the concentration of specific clotting factors is expressed as a percentage of an equine control pool. Reference (normal) values are generally between 50% to 150%. Fibrinogen is the exception. It is measured in mg/dl (g/L).

Fibrinogen is more commonly assessed as an acute phase reactant protein, rather than as a clotting factor.

PROTEINS

Serum protein electrophoresis is useful in the investigation of cases with marked hypoproteinemia and (especially) hyperproteinemia.

Immunoglobulins

Failure of passive transfer is a common entity on breeding farms. A variety of methods exists for assessment of immunoglobulin transfer in the neonate (see Chapter 12.13: "Prematurity"). Failure of passive transfer is usually regarded as confirmed by a serum immunoglobulin G value less than 200 mg/dl (<2.0 g/L) at 24 hours of age. Adequate passive transfer is considered greater than 800 mg/dl (>8.0 g/L). Colostrum with IgG concentration less than 1000 mg/dl (<10 g/L) leads to failure of passive transfer. Specific immunoglobulin concentrations have been reported for foals of various ages and for adult horses. They are infrequently measured in clinical practice.

Acute Phase Reactants

Acute phase reactants are proteins that increase in the blood as part of the systemic response to inflammation.

Their measurement is a useful adjunct to clinical examination, especially when the leukogram does not support a diagnosis of inflammation. Fibrinogen is the most commonly measured; however, others are becoming available, such as C-reactive protein and serum amyloid A.

Fibrinogen

Dehydration may cause a relative hyperfibrinogenemia. Therefore fibrinogen is often assessed relative to total plasma protein (TPP) concentration. A TPP/fibrinogen ratio greater than 15:1 suggests that the increase is caused by dehydration, whereas a ratio less than 10:1 suggests

that the increase is caused by inflammation. Reference values are noted in the Hematology tables in this appendix.

Serum Amyloid A

Reference values for foals are less than 6 mg/dl (<0.06 g/L); values greater than 10 mg/dl (>0.1 g/L) are considered suggestive of infection (Stoneham and colleagues, 2001).

C-Reactive Protein

Reference values for C-reactive protein in horses were reported as 3.4-11.4 µg/ml (3.4-11.4 mg/L). Values mean \pm 2SD, n = 10 (Takiguchi and colleagues, 1990).

Serum Protein Electrophoresis

		LUMSDEN AND COLLEAGUES* (1980)			MATTHEWS† (1982)
		Thoroughbred Mares (n = 60)	Standardbreds (n = 49-50)	Thoroughbred Foals (n = 9-12)	Greater than or Equal to 1 Year Old (n = 30)
Protein, total	g/dl	5.7-7.4	5.3-7.4	5.0-6.1	5.3-7.9
	g/L	57-74	53-74	50-61	53-79
Albumin	g/dl	2.9-3.6	2.7-3.4	2.6-3.2	2.3-3.7
	g/L	29-36	27-34	26-32	23-37
Globulins, total	g/dl	2.6-4.1	2.2-4.3	2.2-3.2	
	g/L	26-41	22-43	22-32	
Albumin:globulin ratio		0.7-1.2	0.7-1.3	0.8-1.5	
Globulin fractions:					
α_1	g/dl	0.5-1.4	0.7-1.7	0.7-1.2	0.4-0.9
	g/L	5-14	7-17	7-12	4-9
α_2	g/dl				0.3-1.0
	g/L				3-10
β_1	g/dl	0.9-1.8	0.6-2.0	0.9-1.2	0.2-1.6
	g/L	9-18	6-20	9-12	2-16
β_2	g/dl				0.2-0.9
	g/L				2-9
γ_1	g/dl	0.6-1.4	0.8-1.6	0.4-1.0	0.1-0.4
	g/L	6-14	8-16	4-10	1-4
γ_2	g/dl				0.3-0.9
	g/L				3-9

All values were obtained by agarose gel electrophoresis.

*Lumsden and colleagues (1980): Thoroughbred and Standardbred values are 2.5 to 97.5 percentiles. Foals were 1 to 6 months old; values are ranges.

†Matthews (1982): Values are mean \pm 2SD.

GASTROINTESTINAL SYSTEM (INCLUDING THE LIVER)

Liver Function Tests

If a chronic hepatopathy is suspected, assessing liver function is appropriate before performing a liver biopsy. Assessing APTT and PT is also worthwhile because clotting factors are produced in the liver. Such tests are likely to be abnormal (prolonged) when more than 70% of the functional hepatic mass has been compromised.

Dye Clearance Studies

Two cholephilic dyes have been used: Bromosulfophthalein (BSP) and indocyanine green (ICG). They are administered by IV injection. Thereafter, at least 3 blood samples are taken from the contralateral jugular vein, usually between 5 and 12 to 15 minutes. Consult your laboratory.

Note that prolonged fasting (3 days) may prolong dye clearance times. Under such circumstances BSP half-life ($T_{1/2}$) was 3.7 to 5.9 minutes and ICG $T_{1/2}$ was 5.1 to 44.7 minutes (Engelking and colleagues, 1985), mean \pm 2SD, n = 10.

BSP Clearance

Engelking and colleagues (1985) used 4.4 to 5.1 mg BSP/kg body weight (bwt). The $T_{1/2}$ was 2.2 to 4.1 minutes, mean \pm 2SD, $n = 10$.

ICG Clearance

Engelking and colleagues (1985) used 0.8-1.1 mg ICG/kg bwt. The $T_{1/2}$ was 5.4 to 13.8 minutes, mean \pm 2SD, $n = 10$. Parry and colleagues (1989) used 45 mg ICG/horse (400-500 kg bwt). The $T_{1/2}$ was 3.1 to 6.9 minutes, ranges, $n = 10$.

Bile Acids

Assessment of serum bile acid concentration (and a bile acid tolerance test) may be an alternative to the above. De-

creased liver function may be associated with increased serum bile acid concentrations.

Plasma ammonia concentration may also increase with decreased liver function. However, because the plasma concentration increases after collection, it is probably less useful in clinical practice.

Serum Lipids and Lipoproteins

Watson and colleagues (1991) provide a good introduction to various lipid and lipoprotein reference values for horses and ponies. They are infrequently measured in clinical practice but may be useful to confirm hyperlipemia in ponies and hyperlipidemia in horses.

Routine Biochemistry Tests: Adults

		LUMSDEN AND COLLEAGUES (1980) ^a		
		Thoroughbred (n = 59-60)	Standardbred (n = 49-50)	Others
Enzymes				
AP (ALP)	U/L 37° C	26-92	24-67	
AST (SGOT)	U/L 37° C	141-330	123-789	
Amylase	U/L 37° C			14-35 ^b
	Caraway U/L 37° C	120-1400	410-1200	
GGT	U/L 30° C			4-44 ^c
	U/L 37° C			9-29 ^b
LDH	U/L 30° C	81-225	74-206	
	U/L 37° C	137-381	125-349	
Lipase	U/L 37° C			23-87 ^b
Sorbitol (Iditol)	U/L 30° C	<5		
dehydrogenase (SDH)	U/L 37° C	<6		3-13 ^d
Nonenzymes				
Ammonia fasting	μg/dl			0-56 ^e
	μmol/L			0-33
Bile acids fasting	μg/ml			0.2-4.5 ^f
	μmol/L			0.5-11.4
Bilirubin				
Total	mg/dl	0.9-2.6	0.9-2.9	
	μmol/L	15-45	15-50	
Unconjugated (U)	mg/dl	0.3-1.7	0.6-2.5	
	μmol/L	5-29	10-43	
Conjugated (C)	mg/dl	0.2-0.8	0.2-0.7	
	μmol/L	3-14	3-12	
U:C ratio	No units	0.7-4.5	0.4-7.5	
Cholesterol	mg/dl	73-138	61-112	
	mmol/L	1.89-3.57	1.58-2.90	
Glucose	mg/dl	69-150	63-101	
	mmol/L	3.8-8.3	3.5-5.6	

AP, Alkaline phosphatase; AST, aspartate aminotransferase; GGT, γ -glutamyl transferase; LDH, lactate dehydrogenase.

^aLumsden and colleagues (1980): Values are 2.5-97.5 percentiles.

^bParry and Crisman (1991): Ranges, $n = 17$.

^cGossett and French (1984): Mean \pm 2SD, $n = 10$.

^dHorney and colleagues (1993): Mean \pm 2SD, $n = 9$.

^eOgilvie and colleagues (1985): Mean \pm 2SD, $n = 11$.

^fHoffman and colleagues (1987): Mean \pm 2SD, $n = 20$.

Routine Biochemistry Tests: Foals

		GOSSETT AND FRENCH (1984)*			
Age		0.5-3 Days	2-3 Weeks	5-7 Weeks	
GGT	U/L 30° C 0-94		0-146	0-48	
SDH	U/L room temperature	0.2-3.8	0-5.3	0-1.5	
		SCHMITZ AND COLLEAGUES (1982)†			
Age		1-2 Days	1-2 Weeks	4-5 Weeks	6 Months
AP	U/L 30° C	530-2611	347-787	284-734	176-348
	U/L 37° C	1104-5440	723-1640	592-1529	367-725
AST	U/L 30°C	24-123	74-229	101-201	111-178
	U/L 37°C	34-176	106-327	144-287	159-254
Total bilirubin	mg/dl	0.8-5.8	1.0-3.4	0.6-2.4	0.5-1.7
	μmol/L	13-99	17-57	10-41	8-29
		BAUER AND COLLEAGUES (1984)‡			
Age		1 Day	1 Week	1 Month	6 Months
Unconjugated bilirubin	mg/dl	0.4-2.8	0.4-1.6	0.2-0.6	0-0.7
	μmol/L	7-48	7-27	3-10	0-12
Conjugated bilirubin	mg/dl	0.2-1.4	0.1-0.9	0-0.7	0-0.7
	μmol/L	3-24	2-15	0-12	0-12
Glucose	mg/dl	108-223	126-198	119-205	81-196
	mmol/L	6.0-12.4	7.0-11.0	6.6-11.4	4.5-10.9

*Gossett and French (1984): Mean ± 2SD, n = 10.

†Schmitz and colleagues (1982): Mean ± 2SD, n = 21-28.

‡Bauer and colleagues (1984): Mean ± 2SD, n = 26.

ELECTROLYTES AND OSMOLALITY

The commonly measured electrolytes are sodium, potassium, and chloride. Calculation of the fractional excretion of electrolytes (based on their plasma and urine concentrations) provides a guide to their homeostasis and to renal function.

Equine RBCs contain a high potassium concentration. Therefore samples should be analyzed as soon as practical after collection, to minimize leakage from RBC and an apparent (spurious) hyperkalemia. The latter may occur before obvious hemolysis.

Serum or plasma potassium concentration does not reliably reflect intracellular (body) status. Measurement of intraerythrocyte potassium concentration may provide a better guide (Muylle and colleagues, 1984a,b) and be a

useful adjunct in determining appropriate fluid therapy in horses with diarrhea and other causes of significant electrolyte loss.

A potassium challenge test has been suggested as a diagnostic aid for horses with suspected hyperkalemic periodic paralysis (Speir and colleagues, 1990; Naylor and colleagues, 1993).

Total CO₂ reflects the acid-base status of an animal. It is about 95% bicarbonate. The anion gap also provides an insight in acid-base balance. It may be calculated as the following:

$$\text{Anion gap} = ([\text{Na}^+] + [\text{K}^+]) - ([\text{Cl}^-] + [\text{TCO}_2])$$

OR

$$\text{Anion gap} = ([\text{Na}^+] + [\text{K}^+]) - ([\text{Cl}^-] + [\text{HCO}_3^-])$$

Electrolytes and Osmolality: Adults

Serum or Plasma		LUMSDEN AND COLLEAGUES ^a (1980)		Others
		Thoroughbreds (n = 59-60)	Standardbreds (n = 49-50)	
Sodium (Na ⁺)	mEq/L	134-142	137-143	
	mmol/L	134-142	137-143	
Potassium (K ⁺)	mEq/L	2.1-4.2	2.9-4.4	
	mmol/L	2.1-4.2	2.9-4.4	
Na ⁺ :K ⁺ ratio		33-66	30-48	
Chloride (Cl ⁻)	mEq/L	94-106	96-102	
	mmol/L	94-106	96-102	
Calcium (Ca ⁺⁺)	mg/dl	10.7-12.4	10.9-12.9	
	mmol/L	2.67-3.09	2.73-3.23	
Ionized calcium (Ca ⁺⁺)	mg/dl			6.01-7.21 ^b
	mmol/L			1.50-1.79
Phosphate (Pi)	mg/dl	1.1-4.4	2.2-4.2	
	mmol/L	0.36-1.42	0.71-1.36	
Ca:Pi ratio		2.5-9.3	2-5	
Magnesium (Mg ⁺)	mg/dl	1.6-2.3	1.7-2.2	
	mmol/L	0.66-0.95	0.70-0.90	
Total CO ₂	mEq/L			27-32 ^c
	mmol/L			27-32
Anion gap	mEq/L			8-13 ^b
	mmol/L			8-13
Osmolality ^d	mosm/kg	279-296	281-292	
	mmol/kg	279-296	281-292	
RBC potassium: ^e				
High K ⁺ group	mEq/L			90-104
	mmol/L			90-104
Low K ⁺ group	mEq/L			77-90
	mmol/L			77-90

^aLumsden and colleagues (1980): 2.5 to 97.5 percentiles.

^bKohn and Brooks (1990): Mean \pm 2SD, n = 39.

^cGossett and French (1983): Mean \pm 2SD; n = 10.

^dLithium heparin as anticoagulant.

^eMuyllé and colleagues (1984a). Horses were arbitrarily divided into "high K⁺" (n = 394) and "low K⁺" (n = 42) groups because the data had a bimodal distribution, with a "section point" at 90 mEq/L (90 mmol/L). Values are ranges.

Electrolytes and Osmolality: Foals

Age		BAUER AND COLLEAGUES (1984)			
		1 Day	1 Week	1 Month	6 Months
Calcium (Ca ⁺⁺)	mg/dl	9.6-13.6	11.2-13.6	11.0-13.4	10.2-13.4
	mmol/L	2.40-3.40	2.80-3.40	2.75-3.35	2.55-3.35
Phosphate (Pi)	mg/dl	3.8-7.4	5.4-9.4	4.9-9.3	4.8-7.6
	mmol/L	1.23-2.39	1.75-3.03	1.57-3.01	1.54-2.46
Ca:Pi ratio (mean)		1.6	1.3	1.3	1.5
Sodium (Na ⁺)	mEq/L	132-156		Applicable to all ages	
	mmol/L	132-156			
Potassium (K ⁺)	mEq/L	3.5-5.5		Applicable to all ages	
	mmol/L	3.5-5.5			
Na:K ratio	(mean)	32.0			
Chloride (Cl ⁻)	mEq/L	94-114		Applicable to all ages	
	mmol/L	94-114			

Electrolytes and Osmolality: Foals—cont'd

Age		BAUER AND COLLEAGUES (1984)			
		1 Day	1 Week	1 Month	6 Months
Total CO ₂ (TCO ₂)	mEq/L mmol/L	21-33 21-33		Applicable to all ages	
Anion gap	mEq/L mmol/L	8-24 8-24	9-25 9-25	13-25 13-25	9-25 9-25

Values are mean \pm 2 SD, n = 26.

Anion gap = $([Na^+] + [K^+]) - ([Cl^-] + [TCO_2])$.

RESTING ACID-BASE AND BLOOD GAS VALUES

The specimen should be collected into a heparinized syringe, and care should be taken to expel any air bubbles before capping the end of the needle and then placing the sample on ice (to keep it at 4° C) until it is analyzed (within 1-3 hours).

With appropriate compensation in acid-base disorders, the following changes are likely to occur (Blackmore and Brobst, 1981; Brobst, 1983):

Acute respiratory acidosis: $[HCO_3^-]$ increases 1 mEq/L (1 mmol/L) for every 10 mm Hg increase in P_{CO_2} .

Chronic respiratory acidosis: $[HCO_3^-]$ increases 3 to 4 mEq/L (3-4 mmol/L) for every 10 mm Hg increase in P_{CO_2} .

Acute respiratory alkalosis: $[HCO_3^-]$ decreases 1 to 3 mEq/L (1 mmol/L) for every 10 mm Hg decrease in P_{CO_2} .

Chronic respiratory alkalosis: $[HCO_3^-]$ decreases 5 mEq/L (1 mmol/L) for every 10 mm Hg decrease in P_{CO_2} .

Metabolic acidosis: P_{CO_2} decreases 1.2 mm Hg for every 1 mEq/L (1 mmol/L) decrease in $[HCO_3^-]$.

Metabolic alkalosis: P_{CO_2} increases 0.6 to 1 mm Hg for every 1 mEq/L (1 mmol/L) increase in $[HCO_3^-]$.

		ARTERIAL		VENOUS
		Aguilera-Tejero and Colleagues (1998) Young Horses Mean \pm 2SD (n = 16)	Aguilera-Tejero and Colleagues (1998) Old Horses Mean \pm 2SD (n = 16)	Soma and Colleagues (1996) Ranges (n = 60)
pH		7.364-7.444	7.372-7.484	7.330-7.410
P_{CO_2}	mm Hg	37-49	34-50	46-64
P_{O_2}	mm Hg	89-115	73-108	
HCO_3^-	mEq/L	23-30	20-34	25-35
	mmol/L			
Base excess	mEq/L			
	mmol/L			-1 to 7

URINARY SYSTEM

A water deprivation test may be performed to evaluate renal tubular concentrating ability. Horses deprived of water for 60 to 72 hours lost 12% to 16% of their body weight and had maximal urine specific gravities of 1.042 to 1.054. Urine osmolalities ranged from 1359 to 1844 mosm/kg and urine/serum osmolality ratios from 4.4 to 6.2 (Brobst and Bayly, 1982).

Fractional Excretion

Fractional excretion (FE) of electrolytes—such as sodium, potassium and chloride—may be useful in the evaluation of renal function (Morris and colleagues, 1984). Similarly, FE of calcium (Ca^{++}) and phosphate (Pi) may be useful guides to their dietary intake (Caple and colleagues, 1982).

Mares fed adequate Ca^{++} had $FE_{Ca^{++}}$ greater than 2.5% and FE_{Pi} less than 4%.

Clearance Studies

Glomerular function is not usually directly evaluated in clinical practice. Holdstock and colleagues (1998) reviewed inulin clearance and creatinine clearance for the assessment of glomerular filtration rate and paraaminohippurate (PAH) clearance for the assessment of renal plasma flow in horses and foals. Taylor and colleagues (1990) reviewed sodium sulphanilate clearance to assess glomerular filtration rate. Morris and colleagues (1984) and Kohn and Strasser (1986) reviewed the literature on creatinine clearance data in horses and ponies and reported clearance data for Na^+ , K^+ , Cl^- , Ca^{++} , and Pi.

Serum or Plasma Biochemistry

LUMSDEN AND COLLEAGUES (1980)			
		Thoroughbreds (n = 60)	Standardbreds (n = 49-50)
Urea (BUN)	mg/dl	11-24	8-14
	mmol/L	4.0-8.6	2.8-5.0
Creatinine	mg/dl	0.9-2.1	0.9-1.7
	μmol/L	80-185	80-150

Values are 2.5 to 97.5 percentiles.

Urine: 24-Hour Collection

Kohn and Strasser (1986) (n = 6)		
Protein		
Total	mg/kg/day	3.6-22.3
Albumin	mg/kg/day	0.2-8.8
Globulin	mg/kg/day	3.4-13.6
Protein: creatinine ratio	No units	0.11-0.60
	g/mmol	0.013-0.068
Creatinine clearance	ml/min/kg	1.49-2.74
Urine output	ml/kg/day	15-25

Values are ranges.

Urinalysis*

	Horse	Foal
Gross Appearance		
Color	Pale yellow to brown	
Viscosity	Viscous (mucoid)	
Transparency	Slightly turbid (turbidity increased by cooling)	
Specific gravity	1.006-1.050 (usually 1.020-1.050) Should be greater than 1.020 if the blood urea concentration is increased	1.001-1.027
Dipstick Chemistries		
pH	7.0-9.0 (usually 7.5-8.5)†	5.5-8.0
Protein‡	None to possibly trace in concentrated urine	Negative to 30 mg/dl
Glucose	None	None
Ketones	None	
Bilirubin	None	
Blood	None§	None to 2+
Sediment Findings (Microscopy)		
Mucus		None to abundant
Casts/LPF	None (possibly rare hyaline cast)	None
RBC/HPF	0-8	None
WBC/HPF	0-8	0-3 (sometimes clumps present)
Epithelial cells/HPF		Squamous cells: none to 2-3 (sometimes clumps present)

HPF, High power field (×400 magnification); LPF, low power field (×100 magnification).

*"Horse" results are based on a review by Kohn and Chew (1987). Foal results are from Brewer and colleagues (1991).

†The pH of urine in Thoroughbreds after racing has a bimodal pattern and ranges from pH 4.5 to 9.5 with peaks at about pH 5 and 8. In Standardbreds it has a unimodal pattern and is usually between pH 7 and 9 (Stanley and colleagues, 1995).

‡Note that false-positive results for protein may occur on dipstick examination of alkaline urine. Such findings should be verified by another method, such as precipitation with sulfosalicylic acid.

§Transient hematuria, pigmenturia (hemoglobinuria or myoglobinuria), and proteinuria are common following strenuous exercise (Schott and colleagues, 1995).

Urinalysis—cont'd

	Horse	Foal
Sediment Findings (Microscopy)—cont'd		
Sperm	May be present in stallion urine	
Bacteria	May be noted in free catch samples, but not in catheterized or cystocentesis ones	Very few may be noted in free catch samples; none in catheterized samples
Crystals	Usually numerous calcium carbonate crystals Sometimes "triple phosphate" crystals present	Usually none Sometimes abundant calcium oxalate or rare amorphous urate crystals present

Fractional Excretion Values

		Morris and Colleagues* (1984)	Genetzky and Colleagues† (1987)
Sodium (Na)	%	0-0.67	0.004-0.34
Potassium (K)	%	24.0-53.0	22.7-59.3
Chloride (Cl)	%	0.53-1.49	0.06-0.73

*Morris and colleagues (1984): All values on 24-hour urine samples, mean \pm 2SD (n = 10).

†Genetzky and colleagues (1987): Random urine samples, values are ranges (n = 12).

MUSCULOSKELETAL SYSTEM**Equine Exercise Physiology**

The biochemical adaptations of the horse to athletic exercise and the alterations which result from various training programs are an important facet of equine sports medicine.

Biochemical and histochemical analysis of muscle fiber biopsies have been undertaken, usually from the middle gluteal muscle. Skeletal muscles are a heterogeneous collection of fiber types. Sampling from different areas of the same muscle will consequently yield different results. Therefore several biopsies from the one animal or single samples from several animals are recommended to detect biochemical changes associated with training.

Routine Biochemistry

Serum or Plasma		LUMSDEN AND COLLEAGUES (1980)	
		Thoroughbreds (n = 59-60)	Standardbreds (n = 49-50)
Enzymes			
AP (ALP)	U/L 37° C	26-92	24-67
AST (GOT)	U/L 37° C	141-330	123-789
CK (CPK)	U/L 37° C	2-147	18-217
LDH	U/L 37° C	137-381	125-349
Nonenzymes			
Calcium (Ca ⁺⁺)		See Electrolytes (p. 876)	
Phosphate		See Electrolytes (p. 876)	
Lactate	mg/dl	2.5-15.5	4.1-11.0
	mEq/L	0.28-1.72	0.46-1.22
	mmol/L	0.28-1.72	0.46-1.22

Values are 2.5 to 97.5 percentiles.

Various workers have studied AP, CK, and LDH isoenzymes; however, they are seldom assessed in clinical practice.

ENDOCRINOLOGY

Endocrinopathies are infrequently evaluated in horses. Reference values will vary with the laboratory that performs the test. The following references serve as an introduction to the literature in this area:

- Aldosterone, angiotensin I (plasma renin activity) and arginine vasopressin (antidiuretic hormone): McKeever and colleagues (1992)

- Epinephrine (adrenaline) and norepinephrine (noradrenaline): González and colleagues (1998)
- Gastrin: Smyth and colleagues (1989)
- Oral glucose tolerance test: Murphy and colleagues (1997)
- Insulin: Reimers and colleagues (1982) and Fowden and colleagues (1984)
- T3 (triiodothyronine) and T4 (thyroxine): Duckett and colleagues (1989) and Sojka and colleagues (1993)

Adrenal-Pituitary Axis

		Reference Values	Reference
Plasma ACTH (Resting)	pg/ml	<55	van der Kolk and colleagues (2001a)
Cortisol: Plasma (Resting)	nmol/L	82-254	van der Kolk and colleagues (2001a)
Cortisol: Plasma (2-hr post-ACTH)	nmol/L	308-602	van der Kolk and colleagues (2001b)
Cortisol: Saliva (Resting)	nmol/L	0.6-2.0	van der Kolk and colleagues (2001b)
Cortisol: Saliva (2-hr post-ACTH)	nmol/L	14.0-30.5	van der Kolk and colleagues (2001b)
Cortisol: Urine	ng/ml	<1000*	Caloni and colleagues (1999)

ACTH, Adrenocorticotrophic hormone.

*The threshold value proposed by the International Conference of Racing Authorities.

CEREBROSPINAL FLUID

Cisternal and lumbar taps produce similar values (Mayhew and colleagues, 1977). Adults have clear and colorless cerebrospinal fluid (CSF), whereas foals at 5 to 11 days of age have clear to hazy and straw-yellow to colorless fluid, but this is clear and colorless by 12 days of age. Protein is usually assessed as total protein, most of which is albumin. The Pandy's test provides a qualitative assessment of immunoglobulin concentration. It is usually graded as negative to trace. Johnson and Constantinescu (2000) discussed the calculation of an albumin quotient (AQ) and IgG index, to assess the integrity of the blood-CSF barrier and production of immunoglobulin in the CSF, respectively. These are not routinely assessed in clinical practice:

$$AQ = \frac{CSF [albumin] \times 100}{Serum [albumin]}$$

Normal CSF albumin concentration is considered to be 150 to 700 mg/L, whereas the AQ was 0 to 2.2.

$$IgG \text{ index} = \frac{CSF [IgG] \times Serum [albumin]}{Serum [IgG] \times CSF [albumin]}$$

Normal CSF IgG index is considered to be 0.1 to 0.3. An increased AQ with a "normal" IgG index may suggest increased permeability of the blood-CSF barrier. A normal AQ and an increased IgG index may suggest increased intrathecal Ig synthesis. Increased AQ and IgG index may suggest increased permeability or hemorrhage and increased intrathecal Ig synthesis.

Creatine kinase is the only enzyme routinely measured in CSF for clinical diagnostic work; increased values suggest neuronal damage or degeneration. Reference values have also been reported for AST (GOT), GGT, and LDH (Mayhew and colleagues, 1977; Rossdale and colleagues, 1982).

Cerebrospinal Fluid

		ADULT	FOAL
		Beech (1983) Ranges (n = 16-23)	Furr and Bender (1994) Ranges (n = 14)
Cytology			
RBC	/μl		0-320
Total nucleated cell count	/μl	0-48 ^a	0-5
Small mononuclear cells	%	60-94	0-43
Large mononuclear cells	%	6-40	0-92
Neutrophils	%	0 ^b	0
Eosinophils	%	0	0
Biochemistry		Mayhew and colleagues (1977)	
CK (CPK)	U/L 37° C	0-8 ^c	
Glucose	mg/dl	30-75 ^d	
	mmol/L	1.7-4.2	
Total protein	mg/dl	5-105 ^e	
	g/L	0.05-1.05	

^aMayhew and colleagues (1977) reported that the total nucleated cell count of CSF was 0 to 6/μl. Many laboratories favor a reference range of 0 to 10/μl.

^bUsually none; 3 animals had "a few" present.

^cRossdale and colleagues (1982) found somewhat higher CK values of 7 to 25 U/L for adults. They also measured CSF CK in clinically normal neonatal foals (<40 hr old): CK 25° C 4 to 39 U/L (37° C 9-90 U/L). They found that values declined to within the adult reference range within about 48 hours. Interestingly, 16 premature (induced) foals (also <40 hr old) had CK values within the adult reference range.

^dMayhew and colleagues (1977) reported that CSF glucose concentration was 35% to 75% of the corresponding blood value. This is lower than the 60% to 80% ratio that is often accepted for other species. It probably reflects the effect of IV injection of xylazine before sample collection, which results in short-term hyperglycemia.

^eIn addition: Beech (1983) reported total protein of 0 to 88 mg/dl (0-0.9 g/L).

Rossdale and colleagues (1982) reported total protein of 40 to 170 mg/dl (0.4-1.7 g/L).

PERITONEAL FLUID

Approximately 5 to 10 ml of peritoneal fluid (PF) can often be collected from normal adult horses within a few minutes. However, sometimes no fluid can be collected, despite repeated attempts at various sites. PF is usually straw-yellow in color but occasionally is clear to orange. It

is usually transparent but occasionally slightly turbid. The following adult cytology reference data are based on Bach (1973), Brownlow (1979), and Nelson (1979). Biochemistry reference data are from Nelson (1979) and Parry and Crisman (1991). The foal reference data are from Grindem and colleagues (1990).

Peritoneal Fluid

Cytology	Units	Adult	Foal
RBC count	×10 ⁶ /L		100-19,900
	×10 ⁹ /L		0.1-19.9
Total nucleated cell count	/μl	<10,000 (often <5,000)	<1400
	×10 ⁹ /l	<10.0 (often <5.0)	<1.4
Neutrophils	%	20-90	2-94
Lymphocytes	%	0-35	0-7 (usually about 1)
Large mononuclear cells	%	5-60 ^a	5-98 ^b
Eosinophils	%	0-5	0-4 (usually 0)
Basophils	%	0-1	0
Total protein	g/dl	<2.5 (usually <1.5)	<2.0
	g/L	<25 (usually <15)	<20

^aThese cells were commonly vacuolated and phagocytic (often of degenerate neutrophils). Occasional mitotic cells were also noted.

^bCells were rarely phagocytic of other cells. On average there were about equal proportions of neutrophils and large mononuclear cells present.

Continued

Peritoneal Fluid—cont'd

Paired Samples		ADULT		FOAL	
		Blood	PF	Blood	PF
Amylase ^c	U/L 37° C	14-35	0-14		
Bilirubin (Total)	mg/dl	0.8-1.5	0.3-0.8		
	μmol/L	13-25	5-13		
Creatinine	mg/dl	1.5-1.8	1.8-2.7		
	μmol/L	133-156	161-237		
GGT ^c	U/L 37° C	9-29	0-6		
Glucose ^d	mg/dl	72-100	89-115		
	mmol/L	4.0-5.6	4.9-6.4		
Lactate ^c	mg/dl	5.8-15.5	3.8-10.9		
	mmol/L	0.6-1.7	0.4-1.2		
Lipase ^e	U/L 37° C	23-87	0-36		
Urea ^f	mg/dl	11-16	13-22	2-14	2-8
	mmol/L	3.9-5.5	4.5-7.8	0.8-4.98	0.83-2.82

PF, Peritoneal fluid.

^cBlood value greater than PF value in all horses.

^dBlood glucose value less than PF value in 95% of horses.

^eBlood lipase value greater than PF value in 95% of horses.

^fPlasma urea value less than or equal to PF value in all foals.

Pleural Fluid

		Range (n = 18)	Comments
Volume			2-8 ml easily collected
Color			Reddish yellow
			Clear to hazy
RBC	×10 ³ /μL	22-540	No erythrophagocytosis
	×10 ⁹ /L	22-540	
Nucleated cell count	/μL	800-12,100	94% of horses were 800-8000/μl
	×10 ⁹ /L	0.8-12.1	(0.8 - 8.0 × 10 ⁹ /L)
Neutrophils	%	32-91	
	/μl	450-10,290	
	×10 ⁹ /L	0.5-10.3	
Lymphocytes	%	0-22	94% of horses were 0-10%
	/μl	0-680	
	×10 ⁹ /L	0-0.7	
Large mononuclear cells	%	5-66	
	μl	50-2620	
	×10 ⁹ /L	0.1-2.6	
Eosinophils	%	0-9	90% of horses were 0%; 5% were 1%;
	/μl	0-170	and 5% were 9% (latter horse was 170/μl,
	×10 ⁹ /L	0-0.2	0.2 × 10 ⁹ /L)
Total protein (Refractometer)	g/dl	0.2-4.7	90% of horses were 0.5-3.4 g/dl
	g/L	2-47	(5-34 g/L)

Data are from Wagner and Bennett (1983).

RESPIRATORY SYSTEM CYTOLOGY

Results are influenced by the method of collection and the site sampled. This may be from the trachea, bronchi, or bronchioles/alveolae, usually by nasopharyngeal or transtracheal routes. The nasopharyngeal approach may result in contamination with cornified and noncornified squamous epithelial cells and their adherent bacteria.

As a generalization, actual cell counts are not necessary in the clinical setting. A subjective assessment of the cellularity of the sample—with separation of the cells according to morphology—is usually adequate.

Tracheobronchial washes have low cellularity and little mucus (Whitwell and Greet, 1984). Total nucleated cell counts are generally less than or equal to 1000/ μ l (1.0×10^9 /L). Many of these cells are ciliated columnar epithelial cells—with some nonciliated columnar cells; goblet cells; and small, often clumped cuboidal cells (also called bronchoalveolar cells). Neutrophils and alveolar macrophages represent many of the remaining cells, but they are also only in low numbers. Some macrophages may be vacuolated and/or phagocytic of debris, fungal elements, pollen, vegetable fibers, and RBC; a few others macrophages may contain hemosiderin granules. Lymphocytes are less common and may be difficult to identify. They are usually classified as mononuclear cells, together with other cells that

are not obviously macrophages. Eosinophils are uncommon, and basophils and plasma cells are rare.

Washes from the deeper airways may have somewhat higher cell counts, although this is not invariably the case. Cytology is often similar to that described previously.

Some variation in cellularity and cytology may be related to the volume of fluid used in the lavage procedure (Sweeney and colleagues 1992). Smaller quantities (50 ml) yield more cells per unit volume of fluid recovered with a greater percentage of neutrophils and lymphocytes than larger volumes (300 ml).

Cytology of tracheobronchial specimens does not necessarily correlate with bronchoalveolar samples—particularly in horses with chronic pulmonary disease (Derksen and colleagues 1989)—and the latter may be more clinically useful.

Tracheobronchial specimens from normal horses are not necessarily sterile. Nonpathogenic and potentially pathogenic bacteria have been isolated from clinically healthy and cytologically normal horses. Fungi may also be seen in some normal animals.

Tracheobronchial aspirates from clinically normal foals may have higher eosinophil and neutrophil percentages than adults have (Crane and colleagues 1989). Thus as with any cytology, results must be interpreted in light of clinical signs.

		TRANSTRACHEAL WASH FLUID*	BRONCHOALVEOLAR LAVAGE FLUID		
Cytology		Christley and Colleagues (1999) Mean \pm 2SD (n = 9)	McGorum and Dixon (1994) Ranges (n = 8)	Dixon and Colleagues (1995) Ranges (n = 30)	Raulo and Colleagues (2001) Values in Ranges (n = 15)
Recovery	ml				140-220
	%				47-73†
Total cells	$\times 10^3$ /ml				18-57
Neutrophils	%	0-41	1-4	0-5	0-6
	$\times 10^3$ /ml				0-28
Lymphocytes	%	3-17	20-51	6-53	27-52
	$\times 10^3$ /ml				75-385
Macrophages	%	45-89‡	36-74	36-84	39-70
	$\times 10^3$ /ml				117-356
Eosinophils	%	0-4	0-1	0-0.3	0-2
	$\times 10^3$ /ml				0-19
Mast cells	%	0	1-12	1-13	0-4
	$\times 10^3$ /ml				0-29
Epithelial cells	%		0-2	Not stated	0
	$\times 10^3$ /ml				0

*Similar results were obtained by a transendoscopic nasotracheal aspiration technique.

†Percentage of the 300 ml infused.

‡Of the macrophages, about 1% to 2% were giant cells and 6% were hemosiderinophages.

BRONCHOALVEOLAR LAVAGE FLUID		
Moore and Colleagues (1997)		
Mean \pm 2 SD (n = 6)		
Inflammatory Markers		
Recovery	ml	125-210
	%	42-70
Total protein	mg/L	11-31
Albumin	mg/L	4-21
IgG	mg/L	4-10
IgA	mg/L	7-14
Prostaglandin E ₂	pmol/L	8-15
6-Ketoprostaglandin F ₁ α	pmol/L	0-4
Procoagulant activity	%	2-3 (range)

SYNOVIAL FLUID

Interest in the measurement of enzymes associated with connective tissue turnover and in cartilage degradation products in the synovial fluid as markers of articular disease is increasing. These include matrix metalloproteinases (Clegg and colleagues, 1998) and cartilage oligomeric matrix protein (COMP), aggrecan, collagen type II, keratan sulfate, and total glycosaminoglycan (Skiöldebrand and colleagues, 2001). Synovial fluid protein carbonyl content, a marker of oxidative injury by reactive oxygen species, has been reported as 0 to 0.059 μ mol/g in normal joint fluid (Dimock and colleagues, 2000).

Measurement of paired blood and synovial fluid urea concentrations is recommended to guide the degree of dilution of synovial fluid (Gough and colleagues, 2002). However, its clinical utility is unproven. Reference values for synovial fluid urea concentration are 2.5 to 7.7 mmol/L, with a blood/synovial fluid urea ratio from 0.75 to 1.17.

COMP has also been evaluated in digital sheath synovial fluid and serum of normal horses. Reference values (mean \pm 2 SD) for digital sheath fluid were 9 to 24 μ g/ml. That of serum depended on the age of the horse, with those less than 2 years of age being 5.4 to 9.4 μ g/ml and of older horses being 0.6 to 1.9 μ g/ml (Smith and Heinegård, 2000).

SYNOVIAL FLUID

Characteristic/Factor	Description
Gross appearance	Synovial fluid is pale yellow in color, clear to occasionally slightly turbid, with a high viscosity. If a drop is allowed to string from the end of a needle, it will form a strand about 5 to 10 cm in length. It does not clot but readily exhibits thixotropism.
Mucin clot test	Usually good but occasionally fair in character
Total red cell count	Very few present ($<1400/\mu$ l; $<1.4 \times 10^9/L$)
Total nucleated cell count	Usually $<500/\mu$ l ($<0.5 \times 10^9/L$); often $<200/\mu$ l ($<0.2 \times 10^9/L$)
Total protein concentration	0.5-2.2 g/dl (5-22 g/L); often <1.2 g/dl (<12 g/L) Most of the protein present is albumin.
Cytology	Usually $<10\%$ neutrophils and $>90\%$ mononuclear cells; about 50% of the latter as lymphoid cells and 50% are large mononuclear cells. Vacuolated (phagocytic) mononuclear cells (macrophages) account for $<10\%$ of all nucleated cells.
Cartilage fragments	Detectable in $\leq 15\%$ of "normal" fluid samples Such fragments are of superficial cartilage (i.e., they lack chondrocytes).
Hyaluronate (hyaluronic acid)	19-191 mg/dl (0.2-1.9 g/L)
Sulfated glycosaminoglycans	4.5 mg/dl (<0.05 g/L)

Data from van Pelt (1962), Persson (1971), Tew (1982, 1983), and Little and colleagues (1990).

Bibliography

- Bach LG: Exfoliative cytology of peritoneal fluid in the horse. In Grunsell CSG, Hill FWG (eds): *The Veterinary Annual 1973*, Bristol, England, John Wright, 1974.
- Bauer JE, Harvey JW, Asquith RL et al: Clinical chemistry values of foals during the first year of life. *Equine Vet J* 1984; 16:361-363.
- Beech J: Cytology of equine cerebrospinal fluid. *Vet Pathol* 1983; 20:553-562.
- Brewer B, Clement SF, Lotz WF et al: Renal clearance, urinary excretion of endogenous substances, and urinary diagnostic indices in healthy neonatal foals. *J Vet Intern Med* 1991; 5:28-33.
- Brobst DF: Pathophysiologic and adaptive changes in acid-base disorders. *J Am Vet Med Assoc* 1983; 183:773-780.
- Brobst DF, Bayly WM: Responses of horses to a water deprivation test. *J Equine Vet Sci* 1982; 2:51.
- Brownlow MA: Abdominal paracentesis in the horse: a clinical evaluation [M Vet Sci thesis], Sydney, Australia, The University of Sydney, 1979.
- Caloni F, Spotti M, Villa R et al: Hydrocortisone levels in the urine and blood of horses treated with ACTH. *Equine Vet J* 1999; 31:273-276.
- Caple IW, Doake PA, Ellis PG: Assessment of the calcium and phosphorus nutrition in horses by analysis of urine. *Aust Vet J* 1982; 58:125-131.
- Christley M, Hodgson DR, Rose RJ et al: Comparison of bacteriology and cytology of tracheal fluid samples collected by percutaneous transtracheal aspiration or via endoscope using a plugged, guarded catheter. *Equine Vet J* 1999; 31:197-202.
- Clegg PD, Coughlan AR, Carter SD: Equine TIMP-1 and TIMP-2: identification, activity and cellular sources. *Equine Vet J* 1998; 30:416-423.
- Crane SA, Ziemer EL, Sweeney CR: Cytologic and bacteriologic evaluation of tracheobronchial aspirates from clinically normal foals. *Am J Vet Res* 1989; 50:2042-2048.
- Derksen FJ, Brown CM, Sonea I et al: Comparison of transtracheal aspirate and bronchoalveolar lavage cytology in 50 horses with chronic lung disease. *Equine Vet J* 1989; 21:23-26.
- Dimock AN, Siciliano PD, McIlwraith CW: Evidence supporting an increased presence of reactive oxygen species in the diseased equine joint. *Equine Vet J* 2000; 32:439-443.
- Dixon PM, Railton DJ, McGorum BC: Equine pulmonary disease: a case control study of 300 referred cases. Part 3. Ancillary diagnostic findings. *Equine Vet J* 1995; 27:428-435.
- Dorner JL, Bass VD: Normal prothrombin times and partial thromboplastin times for the horse, cow and goat. *Vet Med Small Anim Clinician* 1974; 69:647.
- Duckett WM, Manning JP, Weston PG: Thyroid hormone periodicity in healthy adult geldings. *Equine Vet J* 1989; 21:123-125.
- Dybdal NO, Hargreaves KM, Madigan JE et al: Diagnostic testing for pituitary pars intermedia dysfunction in horses. *J Am Vet Med Assoc* 1994; 204:627-632.
- Engelking RL, Anwer S, Lofstedt J: Hepatobiliary transport of indocyanine green and sulfobromophthalein in fed and fasted horses. *Am J Vet Res* 1985; 46:2278-2284.
- Fowden AL, Comline RS, Silver M: Insulin secretion and carbohydrate metabolism during pregnancy in the mare. *Equine Vet J* 1984; 16:239-246.
- Furr MO, Bender H: Cerebrospinal fluid variables in clinically normal foals from birth to 42 days of age. *Am J Vet Res* 1994; 55:781-784.
- Genetzky RM, Loparco FV, Ledet AE: Clinical pathologic alterations in horses during a water deprivation test. *Am J Vet Res* 1987; 48:1007-1011.
- González O, González E, Sánchez C et al: Effect of exercise on erythrocyte β -adrenergic receptors and plasma concentrations of catecholamines and thyroid hormones in Thoroughbred horses. *Equine Vet J* 1998; 30:72-78.
- Gossett KA, French DD: Effect of age on anion gap in clinically normal Quarter horses. *Am J Vet Res* 1983; 44:1744-1745.
- Gossett KA, French DD: Effect of age on liver enzyme activities in serum of healthy Quarter horses. *Am J Vet Res* 1984; 45:354-356.
- Gough MR, Munroe GA, Mayhew IG: Urea as a measure of dilution of equine synovial fluid. *Equine Vet J* 2002; 34:76-79.
- Grindem CB, Fairley NM, Uhlinger CA et al: Peritoneal fluid values from healthy foals. *Equine Vet J* 1990; 22:359-361.
- Harvey JW, Asquith RL, McNulty PK et al: Haematology of foals up to one year old. *Equine Vet J* 1984; 16:347-353.
- Hoffman WE, Baker G, Rieser S et al: Alterations in selected serum biochemical constituents in equids after induced hepatic disease. *Am J Vet Res* 1987; 48:1343-1347.
- Holdstock NB, Ousey JC, Rossdale PD: Glomerular filtration rate, effective renal plasma flow, blood pressure and pulse rate in the equine neonate during the first 10 days *post partum*. *Equine Vet J* 1998; 30:335-343.
- Horney BS, Honor DJ, MacKenzie A et al: Stability of sorbitol dehydrogenase activity in bovine and equine sera. *Vet Clin Pathol* 1993; 22(1):5.
- Jain NC: The horse: normal hematology with comments on response to disease. In Schalm's *Veterinary Hematology*, 4th edition, Philadelphia, Lea & Febiger, 1986.
- Johnson PJ, Constantinescu GM: Analysis of cerebrospinal fluid in horses. *Equine Vet Educ* 2000; 12:13.
- Johnstone IB, Crane S: Haemostatic abnormalities in horses with colic: their prognostic value. *Equine Vet J* 1986; 18:271-274.
- Kohn CW, Brooks CL: Failure of pH to predict ionized calcium percentage in healthy foals. *Am J Vet Res* 1990; 51:1206-1210.
- Kohn CW, Chew DJ: Laboratory diagnosis and characterization of renal disease in horses. *Vet Clin North Am Equine Pract* 1987; 3:585-615.
- Kohn CW, Strasser SL: 24-Hour renal clearance and excretion of endogenous substances in the mare. *Am J Vet Res* 1986; 47:1332-1337.
- Little CB, Hilbert BJ, Wickstrom S et al: Quantitative microanalysis of equine synovial fluid glycosaminoglycan concentration. *Am J Vet Res* 1990; 51:1534-1539.
- Lumsden JH, Rowe R, Mullen K: Hematology and biochemistry reference values for the light horse. *Can J Comp Med* 1980; 44:32.
- Matthews AG: Serum protein electrophoresis in horses and ponies. *Equine Vet J* 1982; 14:322-324.
- Mayhew IG, Whitlock RH, Tasker JB: Equine cerebrospinal fluid: reference values of normal horses. *Am J Vet Res* 1977; 38:1271-1274.
- McGorum BC, Dixon PM: The analysis and interpretation of equine bronchoalveolar lavage fluid (BALF) cytology. *Equine Vet Educ* 1994; 6:203.
- McKeever KH, Hinchcliff KW, Schmall LM et al: Plasma renin activity and aldosterone and vasopressin concentration during incremental treadmill exercise in horses. *Am J Vet Res* 1992; 53:1290-1293.
- Meyers K, Reed S, Keck M et al: Circulating endotoxin-like substance(s) and altered hemostasis in horses with gastrointestinal disorders: an interim report. *Am J Vet Res* 1982; 43:2233-2238.
- Moore BR, Krakowka S, McVey DS et al: Inflammatory markers in bronchoalveolar lavage fluid of Standardbred racehorses with inflammatory airway disease: response to interferon-alpha. *Equine Vet J* 1997; 29:142-147.
- Morris DD, Divers TJ, Whitlock RH: Renal clearance and fractional excretion of electrolytes over a 24-hour period in horses. *Am J Vet Res* 1984; 45:2431-2435.
- Murphy D, Reid SWJ, Love S: The effect of age and diet on the oral glucose tolerance test in ponies. *Equine Vet J* 1997; 29:467-470.

- Muyllé E, van den Hende C, Nuytten J et al: Potassium concentration in equine red blood cells: normal values and correlation with potassium levels in plasma. *Equine Vet J* 1984a; 16:447-449.
- Muyllé E, Nuytten J, van den Hende C et al: Determination of red blood cell potassium content in horses with diarrhoea: a practical approach to therapy. *Equine Vet J* 1984b; 16:450-452.
- Naylor JM, Jones V, Berry S-L: Clinical syndrome and diagnosis of hyperkalemic periodic paralysis in Quarter Horses. *Equine Vet J* 1993; 25:227-232.
- Nelson AW: Analysis of equine peritoneal fluid. *Vet Clin North Am Large Anim Pract* 1979; 1:267-274.
- Ogilvie GK, Engelking LR, Anwer MS: Effects of plasma sample storage on blood ammonia, bilirubin, and urea nitrogen concentrations: cats and horses. *Am J Vet Res* 1985; 46:2619-2622.
- Parry BW, Crisman MV: Serum and peritoneal fluid amylase and lipase reference values in horses. *Equine Vet J* 1991; 23:390-391.
- Parry BW, Bayly WM, Tarr B: Indocyanine green clearance and estimation of plasma volume in the normal horse. *Equine Vet J* 1989; 21:142-144.
- Persson L: On the synovia in horses: a clinical and experimental study. *Acta Vet Scand* 1971; 35(Suppl):3-77.
- Raulo SM, Sorsa T, Tervahartiala T et al: MMP-9 as a marker of inflammation in tracheal epithelial lining fluid (TELF) and in bronchoalveolar fluid (BALF) of COPD horses. *Equine Vet J* 2001; 33:128-136.
- Rossdale, PD, Cash RSG, Leadon DP et al: Biochemical constituents of cerebrospinal fluid in premature and full term foals. *Equine Vet J* 1982; 14:134-138.
- Schmitz DG, Joyce JR, Reagor JC: Serum biochemical values in Quarter horse foals in the first 6 months of life. *Equine Pract* 1982; 4(9):24.
- Schott HC, Hodgson DR, Bayly WM: Haematuria, pigmenturia and proteinuria in exercising horses. *Equine Vet J* 1995; 27:67-72.
- Skiöldebrand E, Lorenzo P, Zunino L et al: Concentration of collagen, aggrecan and cartilage oligomeric matrix protein (COMP) in synovial fluid from equine middle carpal joints. *Equine Vet J* 2001; 33:394-402.
- Smith RKW, Heinegård D: Cartilage oligomeric matrix protein (COMP) levels in digital sheath synovial fluid and serum with tendon injury. *Equine Vet J* 2000; 32:52-58.
- Smyth GB, Young DW, Schumacher J: Postprandial serum gastrin concentrations in normal foals. *Equine Vet J* 1989; 21:285-287.
- Sojka JE, Johnson MA, Bottoms GD: Serum triiodothyronine, total thyroxine, and free thyroxine concentrations in horses. *Am J Vet Res* 1993; 54:52-55.
- Soma LR, Uboh CE, Nann L et al: Prerace venous blood acid-base values in Standardbred horses. *Equine Vet J* 1996; 28:390-396.
- Speir SJ, Carlson GP, Holliday TA et al: Hyperkalemic periodic paralysis in horses. *J Am Vet Med Assoc* 1990; 197:1009-1017.
- Stanley SD, Sams RA, Harkins JD et al: Frequency distribution of post race urine pH from Standardbreds compared with Thoroughbreds: research and regulatory significance. *Equine Vet J* 1995; 27:471.
- Stephens KA, Morcom E, Hood DM: Measurement of plasma antithrombin III activity in healthy horses. *Am J Vet Res* 1984; 45:351-353.
- Stoneham SJ, Palmer L, Cash R et al: Measurement of serum amyloid A in the neonatal foal using a latex agglutination immunoturbidimetric assay: determination of the normal range, variation with age and response to disease. *Equine Vet J* 2001; 33:599-603.
- Sweeney CR, Rossier Y, Ziemer EL et al: Effects of lung site and fluid volume on results of bronchoalveolar lavage fluid analysis in horses. *Am J Vet Res* 1992; 53:1376-1379.
- Takiguchi M, Fujinaga T, Naiki M et al: Isolation, characterization, and quantitative analysis of C-reactive protein from horses. *Am J Vet Res* 1990; 51:1215-1220.
- Taylor FGR, Hillyer MH, Lowrey PA: The assessment of glomerular filtration rate in ponies and horses by sodium sulphathiazole clearance. *Equine Vet Educ* 1990; 2:137.
- Tew WP: Demonstration by synovial fluid analysis of the efficacy in horses of an investigational drug (L-1016). *J Equine Vet Sci* 1982; 2:42.
- Tew WP: Synovial fluid analysis: applications in equine joint injury and disease. *Proceedings of the 28th Annual Meeting of the American Association of Equine Practitioners*, p 121, 1983.
- van der Kolk JH, Ijzer J, Overgaauw PAM et al: Pituitary-independent Cushing's syndrome in a horse. *Equine Vet J* 2001a; 33:110-112.
- van der Kolk JH, Nachreiner RF, Schott HC et al: Salivary and plasma concentration of cortisol in normal horses and horses with Cushing's disease. *Equine Vet J* 2001b; 33:211-213.
- van Pelt RW: Properties of equine synovial fluid. *J Am Vet Med Assoc* 1962; 141:1051.
- Wagner AE, Bennett DG: Analysis of equine thoracic fluid. *Vet Clin Pathol* 1983; 11(1):13.
- Watson TDG, Burns L, Love S et al: The isolation, characterisation and quantification of the equine plasma lipoproteins. *Equine Vet J* 1991; 23:353-359.
- Weiser MG: Erythrocyte volume distribution analysis in healthy dogs, cats, horses, and dairy cows. *Am J Vet Res* 1982; 43:163-166.
- Whitwell KE, Greet TRC: Collection and evaluation of tracheo-bronchial washes in the horse. *Equine Vet J* 1984; 16:499-508.

Index

A

AAEP. *See* American Association of Equine Practitioners (AAEP)
AAFCO. *See* Association of American Feed Control Officials (AAFCO)

Abdomen
hemorrhages of, 327
laparoscopic evaluation of, 149-150
ultrasonographic evaluation of, 148-149

Abdominal lavage
for peritonitis without intestinal rupture, 155
via ventral midline celiotomy, 157
Abdominal palpation per rectum, 155
Abdominal paracentesis. *See* Abdominocentesis

Abdominal radiography
for colic in foals, 683-684
for uroperitoneum, 858

Abdominal ultrasonography, 148-149, 155
for ileocecal intussusception, 682f
for intestinal volvulus, 682f
for uroperitoneum, 858

Abdominal wall
hernias of, 310-311
causing dystocia, 320

Abdominocentesis, 149
determining sites for, 155
for rectal tears, 152
in peritonitis, 154-155
in uterine torsion, 312

Abnormal adventitious sounds, 575-576
Abnormal differential cell counts, 409-410
Abnormal maternal-foal behavior, 264-265

Abnormal menace response, 773
Abnormal nutrition, 705

Abnormal ocular discharge, 488-492
diagnosis of, 491

Abortion
caused by equine herpesvirus, 40-41
causing retained fetal membranes, 330
during late gestation, 297
placental evaluation after, 298
prevention of in endotoxemic mares, 108
with placentitis, 298f

Abscesses, 66
in anaerobic pleuropneumonia, 422f
Absolute polycythemia, 358
Acarial infestations, 189
Acclimate, 319
Accommodation, 456
Accumulator species, 801
ACD. *See* Anemia of chronic disease (ACD)

ACE inhibitors. *See* Angiotensin-converting enzyme (ACE) inhibitors

Acetpromazine, 17, 77
detection of, 32
for ergopeptide alkaloid toxicosis, 797
for esophageal obstruction, 93
for forebrain disease, 769
for ileus, 110
for incontinence, 825
for neonatal sedation, 5
for penile paralysis, 304
for perinatal asphyxia syndrome, 647

Acer rubrum leaves. *See* Wilted red maple (*Acer rubrum*) leaves

Acetazolamide for glaucoma, 487

Acetic acid wipes for equine pastern dermatitis, 202

Acetylcholine (ACTH)
challenge for premature foals, 642
stimulating postganglionic fibers, 109

Acetylcysteine, 68
for corneal lacerations, 465
for meconium impaction, 5
for ocular emergencies, 463t

Acetylsalicylic acid. *See* Aspirin (acetylsalicylic acid)

Achilles tendon, examination of, 496
Acid-base balance in dehydration, 119

Acid-citrate-dextrose, 356

Acids, causing corneal ulcers, 466

Acoustic impedance, 564t

Acquired coagulation disorders, 353-354

Acquired immunodeficiencies, 696

Acquired myasthenia gravis, diagnosis of, 744
Acquired pericardial disease, 622-623
Acquired sheared heels, 529
Acquired valvular heart disease, 613-619

Acremonium coenophialum, 796

Acremonium-infected fescue forage, 633

Acroptilon repens, 781

ACTH. *See* Acetylcholine (ACTH)

Actinic keratosis, 480

Actinobacillus, 851
in foal pneumonia, 666, 671
in foals, 3
in jugular vein thrombophlebitis, 626

Actinobacillus equi, 6

Actinobacillus equuli, 838

Actinobacillus lignieresii in thoroughbred racehorses, 414

Actinomyces, 792

Activated charcoal
for cantharidin toxicosis, 785-786
for oxidative erythrocyte damage, 344

Activated macrophages, 228

Activated partial thromboplastin time (APTT), 171

Acupressure, 569

Acupuncture, 569
with interspinous injections, 571

Acute blood loss, 340-341

Acute cholangiohepatitis, 170

Acute intravascular hemolysis, 338

Acute ionophore toxicity, differentiation of, 743t

Acute lung injury (ALI), 427

Acute ocular pain, 462

Acute renal failure, 839-844

causes of, 840b
clinical signs of, 841
diagnosis of, 841-842
etiopathogenesis of, 839-840
prognosis of, 844
therapy of, 842-843

Acute respiratory distress syndrome (ARDS), 427, 674-676

causes of, 427b
clinical signs of, 675-676
diagnosis of, 675-676
etiopathogenesis of, 674-675
pathologic findings, 675
prevention of, 676
prognosis of, 676
treatment of, 676

Acute selenosis, clinical signs of, 802

Acutely ill horse
diet history, 705
energy and protein requirements, 707
enteral feeding of, 708-710
feed assessment, 705-706
feeding protocol
development of, 706
instituting nutritional support
timing of, 707-708
nutritional intervention, 708

Acyclovir
for EHV-1 myelitis, 754, 770
for EHV-1 myeloencephalitis, 752
for equine herpesvirus
myeloencephalopathy, 40
for herpetic keratitis, 476

ADAF. *See* Axial deviation of the aryepiglottic folds (ADAF)

Adenosine triphosphate during ischemia, 135

Adenoviral bronchopneumonia of foals, 697

Adenovirus causing weanling diarrhea, 165

Adequan, 557, 560-561

ADH. *See* Antidiuretic hormone (ADH)

Adhesive tape for foot, 547

Adjustable focusing, 456

Adnexa
extranodal lymphoma of, 360
slit lamp biomicroscope examination of, 450

Adonis aestivalis, 783

ADR. *See* Adverse drug reactions (ADR)

Alpha₂-adrenergic agonists
for colic, 115-116
for large colon impaction, 133
in critical care, 20
increasing upper airway resistance, 391
side effects of, 116

Beta₂-adrenergic agonists, 419

Beta₂-adrenoceptor agonists
for recurrent airway obstruction, 441-442

Adventitious sounds, abnormal, 575-576
Adverse drug reactions (ADR), cutaneous reaction patterns with, 177-178
Adverse drug reactions, manifesting as cutaneous eruptions, 90

Aedes, 48

*Page numbers followed by *f* indicate figures; *t* indicates tables; and *b* indicates boxes.

- Aerobic bacterial cultures for semen evaluation, 269
- Aerobic bacterial pathogens with foal diarrhea, 679
- Aerobic capacity, determination of, 413
- AeroMask, 439
- Aeromonas* causing enteritis, 167
- Aeromonas hydrophila* in foal diarrhea, 679
- Aerophagia, 652
- Aerosolized antimicrobial agents, 437
- Aerosolized bronchodilators, 440-445
- Aerosolized drug delivery devices, 436-440
- disadvantages of, 437
- Aerosolized medications
- for heaves, 420
- recommended dosages for, 441t
- Aerosols, definition of, 437
- Aflatoxicosis, 794-795
- African horse sickness, vectors for, 193
- Agammaglobulinemia in foals, 695
- Agar gel immunodiffusion (AGID) test, 46
- for *Rhodococcus equi* infections, 61
- Age
- and endometrial cysts, 231
- and inability to clear uterus, 234
- and oocyte viability, 277
- and ovarian senescence, 261
- and tapeworm infection, 158
- Agenesis, 827-828
- Aggrecan assays
- for cartilage degradation, 514-515
- for cartilage synthesis, 517
- Aggrecan core protein, 515-516
- Aggrecanase, 515-516
- AGID. *See* Agar gel immunodiffusion (AGID)
- Agkistrodon piscivorus*. *See* Cottonmouth (*Agkistrodon piscivorus*)
- Agkistrodon* spp. *See* Copperhead (*Agkistrodon* spp.)
- AI. *See* Artificial insemination (AI)
- Aimes media, 230
- Airway
- establishment of prior to anesthesia in foals, 690
- inflammation of and exercise-induced pulmonary hemorrhage, 430
- management of in cardiopulmonary resuscitation of newborn foal, 651-652
- obstruction of, 414
- Airway hyperreactivity, 413
- in non-racehorses with cough, 416
- viral infection in, 414
- Albumin in neonates, 3
- Albuterol
- for foal pneumonia, 673
- for heaves, 419
- for placental hydrops, 302
- for recurrent airway obstruction, 444
- formulation of, 439
- Alcohols, 25
- Aldehydes, 25
- Aldosterone, 131
- Alfalfa hay, 89, 99
- beetles in, 784
- mineral content of, 721t
- Alfalfa/casein enteral formulation, 709t
- Algiderm for thermal burns, 222-223
- Algometry, 568
- ALI. *See* Acute lung injury (ALI)
- Alkali disease, 802
- front hoof in, 803f
- Alkaline phosphatase, 176
- Alkalis causing corneal ulcers, 466
- Alkaloids causing interstitial pneumonia, 426
- Alkeran. *See* Melphalan (Alkeran)
- Allantoamnion, 297
- Allantochorion, 297
- Allergen testing, sites for, 184-185
- Allergenic extracts, purchase of, 184
- Allergens, standard concentrations of, 184
- Allergic airway disease, 413
- Allergic dermatitis, 174
- Allergic phenomena, 413
- Allogenic equine erythrocytes, 355
- Alloimmune thrombocytopenia of neonates, 349
- ALOKA 500 SSD, 288
- Alopecia areata, 215-216
- Alphavirus, 766
- Alphavirus encephalitides, 47-49
- clinical signs of, 48
- diagnosis of, 48-49
- epidemiology of, 47-48
- pathology of, 49
- prevention of, 49
- Alsike clover, 768
- Alsike clover poisoning, 790-791
- Alternaria*, 477
- Altrenogest
- causing estrus onset delay, 249-250
- for placental hydrops, 302
- for placentitis, 300
- for recipient mares, 279
- for transvaginal reduction, 247
- Aluminum acetate for equine pastern dermatitis, 202
- Aluminum hydroxide for gastric ulcers, 96
- Ambulatory echocardiography
- for respiratory sinus arrhythmia in thoroughbred horses, 605f
- for ventricular tachycardia, 612f
- Ambulatory electrocardiography for atrial fibrillation, 609f
- AMDUCA. *See* Animal Medicinal Drug Use Clarification Act (AMDUCA)
- American Association of Equine Practitioners (AAEP) on compounding drugs, 31
- American Saddlebred, 384
- glaucoma in, 486
- American Veterinary Medical Association (AVMA) on compounding drugs, 31
- Amicar. *See* Epsilon-aminocaproic acid (Amicar)
- Amikacin, 6
- dosage optimization of, 9
- dosing regimen of, 852t
- for *Clostridium difficile* infection, 168
- for foal pneumonia, 671
- for neonatal septicemia, 3, 660, 661t
- for ocular emergencies, 463t
- for perinatal asphyxia syndrome, 648t
- for peritonitis, 156
- for retained fetal membranes, 332
- for uroperitoneum, 858
- in NFDSM-G extender formulation, 267
- nephrotoxicity of, 4
- Amino acids in parenteral nutrition, 113
- Aminocaproic acid for postpartum hemorrhage, 330
- Aminocaproic acid in critical care, 21
- Aminoglycosides
- avoidance of, 745
- dosage optimization of, 9
- Aminoglycosides—cont'd
- for *Clostridium difficile* infection, 168
- for cystitis, 838
- for duodenitis-proximal jejunitis, 123
- for foal diarrhea, 679
- for foal pneumonia, 671
- for jugular vein thrombophlebitis, 626
- for neonatal septicemia, 3
- for peritonitis, 156
- for pleuropneumonia, 424
- for retained fetal membranes, 332
- neonatal volume of distribution, 3
- nephrotoxicity of, 4, 842
- Aminopenicillin, 6
- oral administration of, 7
- Aminophylline (Cyanamide)
- for foal pneumonia, 673
- for heaves, 419
- for interstitial pneumonia, 428
- Aminopyrine test, 170
- Amiodarone in human cardiopulmonary resuscitation, 655
- Amitraz causing large colon impaction, 131
- Ammonium chloride for cystitis, 838
- Amniotic membranes, inspection of, 324
- Amoxicillin, oral administration of, 7
- Amoxicillin-clavulanate, 6
- Amphotericin B (Fungizone), 479t
- for ocular emergencies, 463t
- Ampicillin, 6
- for neonatal septicemia, 3, 660, 661t
- for proliferative enteropathy, 165
- for retained fetal membranes, 332
- oral administration of, 7
- Amsinckia*, 768, 788, 789
- Amylopectin for equine pastern dermatitis, 202
- Anabolic steroids
- effect on ovaries, 261
- for chronic renal failure, 847
- Anaerobes in foals, 3
- Anaerobic abscess, dental, 374
- Anaerobic bacterial pathogens with foal diarrhea, 678-679
- Anaerobic pleuropneumonia
- abscess in, 422f
- treatment of, 424
- Anal hypotonia, 755
- Analgesics
- for colic, 115-116, 116t
- in foals, 686
- for eyelid lacerations, 465
- for globe proptosis, 464
- for ileal impaction, 128
- for large colon impaction, 133
- for ocular emergencies, 463t
- for small intestine strangulating obstruction, 124
- in critical care, 20
- Anaplasma phagocytophilia*, 54, 89, 345, 349
- causing enteritis, 167
- inclusions, 79f
- Anechoic pleural fluid, sonographic appearance of, 421f
- Anemia
- blood loss in, 336
- clinical signs of, 336-37
- definition of, 336
- diagnosis of, 337-339, 338t
- due to bone marrow aplasia, 343
- due to myelophthisis, 343
- hemolysis in, 336-337
- in foals, 696-697

- Anemia—cont'd
in neonatal isoerythrolysis, 636-637, 639
secondary to inadequate erythropoiesis, 342-343
with right dorsal colitis, 142
Anemia of chronic disease (ACD), 342
Anesthesia
for ocular emergencies, 463t
for ophthalmic examination, 451
induction of
drugs for, 18-19
injectable techniques for, 18t
Anestrous mares, artificial lighting for, 238t
Angiography of thromboembolism, 627
Angiosis, 235
Angiotensin-converting enzyme (ACE) inhibitors
for aortic regurgitation, 618
for ventricular ectopic beats, 611
Angiotropism, 389
Angular limb deformities, 663-665
assessment of, 663-664
classification of, 663
complications associated with, 665
etiology of, 663
treatment of, 664-665
Angulated hocks, 499
Anhidrosis, 816-818
clinical signs of, 816-817
diagnosis of, 817
treatment of, 817-818
Animal and Plant Health Inspection Service (APHIS), 90
Animal Medicinal Drug Use Clarification Act (AMDUCA), 31
Anisocoria, 452
Anoplocephala mamillana, 160
Anoplocephala perfoliata, 128, 138, 158-159
Anorexia, 802
in uterine torsion, 312
Anovulatory follicles with enlarged ovaries, 261
Antacids
for gastric ulcers, 96
oral administration of, 7
Ante mortem diagnosis of lymphoma, 360-361
Anterior chamber
examination of, 453
slit lamp biomicroscope examination of, 450
Anterior enteritis, 120
Anterior synechia, 466
Anterior uveitis, 476
Anterior vitreous, slit lamp biomicroscope examination of, 450
Anthelmintic drugs
for cutaneous habronemiasis, 305
for idiopathic eosinophilic enterocolitis, 147
for multisystemic eosinophilic epitheliotropic disease, 147
for resistant cyathostomiasis, 162-163
Anthelmintics
adverse effects of, 100
avoidance of, 162
classes of, 161
for brainstem disease, 777
Antibacterial cream for thermal burns, 222
Antibacterial shampoo, 199
Antibiotic prophylaxis
for permanent tracheostomy in standing horses, 397
for retained fetal membranes, 332
Antibiotics
dosage of, 9t
for abdominal laparoscopy, 149
for chronic laminitis, 526
for *Clostridium difficile* infection, 168
for corneal lacerations, 465
for corneal ulcers, 466
for duodenitis-proximal jejunitis, 123
for EHV-1 myeloencephalitis, 752
for equine influenza, 43
for equine recurrent uveitis, 470
for eyelid lacerations, 465
for foal pneumonia, 671-672
for fungal keratitis, 478
for globe proptosis, 464
for guttural pouch empyema, 387
for neonatal septicemia, 660
for neonates, 3-4
for osseous sequestra, 538-539
for osteomyelitis of distal phalanx, 526
for perinatal asphyxia syndrome, 648t
for placentitis, 300
for postpartum hemorrhage, 330
for spermatozoa, 267
for stromal abscess, 466
for ulcerative keratomycosis, 466
for uroperitoneum, 858
for uveal injuries, 466
subconjunctival injection of, 459
to prevent cellulitis, 304
234CEQ antibody, 518
Antibody immunohistochemical for interstitial pneumonia, 425
Anticholinergic drugs
for heaves, 419
for recurrent airway obstruction, 442
Anticoagulants for jugular vein thrombophlebitis, 626
Anticollagenolytics
for corneal lacerations, 465
for corneal ulcers, 466
for ocular emergencies, 463t
Anticonvulsive agents
commonly used, 769t
for perinatal asphyxia syndrome, 647
for sick neonatal foals, 640
Antidiuretic hormone (ADH), 829
Antidotoxins, for peritonitis, 156
Antifibrinolytic agents
for acute blood loss, 341
Antifungals, 479t
for fungal keratitis, 478
for ocular emergencies, 463t
for ulcerative keratomycosis, 466
Antihistamines
definition of, 185
for atopic dermatitis, 182-183, 183
interfering with skin test results, 182
Antiinflammatories
for axial deviation of the aryepiglottic folds, 380
for brainstem disease, 777
for cervical stenotic myelopathy, 748
for cutaneous habronemiasis, 196, 305
for equine recurrent uveitis, 470
for eyelid lacerations, 465
for fetal compromise, 632
for glaucoma, 487
for globe proptosis, 464
for hydroceles, 307
Antiinflammatories—cont'd
for interstitial pneumonia, 428
for negative-pressure pulmonary edema, 393
for neonates, 4-5
for neuritis, 476
for ocular emergencies, 464, 464t
for peripheral nerve disease, 739
for peritonitis
monitoring of, 157
without intestinal rupture, 155-156
for permanent tracheostomy in standing horses, 397
for placental hydrops, 302
for placentitis, 300
for pleuropneumonia, 424
for retained fetal membranes, 332
for spinal cord trauma, 749
for upper respiratory tract postoperative management, 395
for viral encephalitis, 770
in critical care, 19-20
Antimicrobials, 6-11
aerosolized, 437
for acquired pericardial disease, 623
for arytenoid chondrosis, 382
for axial deviation of the aryepiglottic folds, 380
for brainstem disease, 777
for endometrial culture, 230-231
for endotoxemia, 108
for equine pastern dermatitis, 202
for fetal compromise, 632
for intrauterine use, 230t
for multisystemic eosinophilic epitheliotropic disease, 147
for neonatal septicemia, 661t
for neonates, 3-4
for perineal lacerations, 333
for peritonitis
monitoring of, 157
without intestinal rupture, 155-156
for placental hydrops, 302
for rectal prolapse, 325
in critical care, 20-21
Antineoplastic agents for lymphoma, 361
Antinuclear antibody (ANA), 177
Antioxidants, 802
for brainstem disease, 777
for spinal cord trauma, 749
Antiprotozoals
for equine protozoal myeloencephalitis, 72-73
for lower motor neuron disease, 752
Anti-Sarcocystis neuroma, 759
Antiseborrheic shampoo, 199
Antiseptics causing corneal ulcers, 466
Antishock therapy, 222
Antisperm antibody assays, 272
Antithrombin III in aerosol, 437
Antitussive agents for heaves, 420
Antivirals for herpetic keratitis, 475
Anxiolytics for inadequate libido, 317
Aorta
bacterial endocarditis of, 618
fetal diameter of, 632
origin of, 592
Aortic aneurysms, 624
Aortic regurgitation, 617-619
Aortic root
aneurysms of, 624
disease of, 624-625
mineralization of, 629

- Aortic valve
auscultation of, 575
echocardiography, 581f
- Aortocardiac fistulas, 624-625
- Aortoiliac thromboembolism, diagnosis of, 627
- Apex beat, 575
- APHIS. *See* Animal and Plant Health Inspection Service (APHIS)
- Aplasia cutis, 219
- Aplastic anemia, 343
- Aplopappus*, 783
- Apocynum*, 783
- Apoptosis, 177
- Appaloosa racing, 429
- Appaloosas
alopecia areata in, 215
cecal impaction in, 138
equine degenerative myeloencephalopathy in, 748
glaucoma in, 487
hyperelastosis cutis in, 219
squamous cell carcinoma in, 480
- APTT. *See* Activated partial thromboplastin time (APTT)
- Aquapuncture, 569
- Aqueous flare, 474
turbidity of, 453
- Aqueous fluid, opacity of, 450
- Aqueous humor and intraocular pressure, 486
- Arab racing, 429
- Arabians
axial deviation of the aryepiglottic folds in, 379
epistaxis in
incidence of, 430
with exercise-induced pulmonary hemorrhage, 429-430
equine degenerative myeloencephalopathy in, 748
glaucoma in, 486
hemophilia A in, 351
rectal tears of, 151
recurrent exertional rhabdomyolysis in, 728
selective immunoglobulin M deficiency in, 696
severe combined immunodeficiency in, 696
with atopy, 181
with cecal impaction, 138
with hematuria, 856
- Arachidonic acid, 420
- ARAS. *See* Ascending reticular activating system (ARAS)
- Arboviruses, control of, 770
- Argentina, embryo transfers in, 277
- Arginase, 176
- Arginine in parenteral nutrition, 113
- Argyle Trocar Thoracic Catheter, 156
- Arnica montana*, 570
- Arquel. *See* Meclofenamic acid (Arquel)
- Arrhythmias
cardiac examination of, 588-589
exercise effect on electrocardiography, 578f
in foals with colic, 681
- Arterial oxygen tension in foals, 688
- Arterial partial pressure in foals, 688
- Arteries
rupture of, 628-629
in mares, 327
temperature, 503
- Arteriovenous fistula, 628
- Arteritis, 629-630
- Arterivirus*, 363-364
- Arthrocentesis of septic joint, 658
- Arthrodesis of distal tarsal joints, 540-543
- Arthrography using magnetic resonance imaging, 509
- Arthropod hypersensitivity, 184-186
treatment of, 185-186
- Arthroscopic fluid delivery system, 156
- Arthroscopy vs. flexible endoscope, 372
- Arthrosis, nuclear scintigraphy of, 501
- Artifacts
during thermography, 504
in tracheal aspirates, 405-406
- Artificial breeding of stallions, 252-256
- Artificial insemination (AI), 252-256
breeding-related problems, 255-256
deep uterine, 275
donor mares for, selection and management of, 277-278
mare preparation for, 272-273
optimizing pregnancy rates, 274-275
pipette for, 273f, 283
recipients of, selection and management of, 278-279
timing of, 275-276
with cooled semen, dosage of, 275
with frozen semen
dosage of, 275
protocol for, 276t
with shipped semen, 271-272
- Artificial lighting
deleterious effects of, 239
in anestrous mares, 238t
- Artificial skin substitutes, 223
- Artificial vagina for semen collection, 254
preparation of, 267
- Arytenoid chondritis, 397
causing postanesthetic upper respiratory tract obstruction, 391
- Arytenoid chondrosis, 381-383
diagnosis of, 381-382
prognosis of, 383
treatment of, 382-383
vs. uncomplicated laryngeal hemiplegia, 381-382
- Arytenoid granulation tissue
laser surgery of, 395-396
- Arytenoidectomy, 382-383, 386
- Arytenoids
chondropathy of, 381f
examination of, 367
- Ascending colon volvulus, 136-137
- Ascending reticular activating system (ARAS), 764, 772
- Asclepias*, 783
- Ascorbic acid (Vitamin C)
for oxidative erythrocyte damage, 344-345
for perinatal asphyxia syndrome, 647, 648t
in parenteral nutrition, 113
- ASD. *See* Atrial septal defects (ASD)
- Aspartate aminotransferase (AST), 169, 176, 762
- Aspergillus*, 792
causing interstitial pneumonia, 426
causing placentitis, 297
- Aspergillus flavus*, 793, 794
- Aspergillus fumigatus*, 389
- Aspergillus nidulans*, 792
- Aspergillus niger*, 793
- Aspergillus parasiticus*, 794
- Asphyxia, adverse effects upon cardiopulmonary function, 646
- Aspiration pneumonia, 800
complicating arytenoidectomy, 383
- Aspirin (Acetylsalicylic acid), 12
for EHV-1 myeloencephalitis, 752
for endotoxemia, 108
for equine recurrent uveitis, 470
for joint disease, 559
- Association of American Feed Control Officials (AAFCO), 26
- AST. *See* Aspartate aminotransferase (AST)
- Astragalus*, 767
- Asystole, 654
- Ataxia associated with cervical spinal cord disease, 746-750
- Atelectatic lung, 421
- Athletic horses
bronchoalveolar lavage of, 409f
globule leukocyte, 410
stifle soreness in, 499
with inflammatory airway disease, 407
with lung abscesses, 408
with parapneumonic effusion, 408
- Athletic performance. *See* Performance
- Atopic dermatitis, 181
treatment of, 182-183
- Atopy, 181-183
clinical signs of, 181
diagnostic tests for, 181-182
differential diagnosis of, 181-182
history of, 181
treatment of, 182-183
- Atrial complexes, 602
- Atrial fibrillation, 574, 605-610
ambulatory electrocardiogram of, 609f
cardiopulmonary resuscitation of newborn foal, 654
clinical signs of, 606
further investigations of, 606-607
mechanisms of, 605-606
posttreatment management of, 608
prognosis of, 606
quinidine sulfate for, complications of, 607-608
uncomplicated, 607
with congestive heart failure, 609-610
with mitral regurgitation, 615
- Atrial septal defects (ASD), 592, 592f, 601
- Atrioventricular block, 603-604, 604-605
in Arab mare
base-apex electrocardiogram of, 606f
in thoroughbred
postexercise electrocardiogram of, 605f
- Atrioventricular dissociation, 574
- Atrioventricular valves, malformation of, 592
- Atropine
for cardiopulmonary resuscitation of newborn foal, 654
for cutaneous habronemiasis, 305
for dysrhythmias, 605
doses of, 604t
for glaucoma, 487
for ocular emergencies, 464t
for posterior segment examination, 453
subconjunctival injection of, 459
- Atropine ophthalmic ointment for herpetic keratitis, 476
- Atypical interstitial pneumonia, 675
- Atypical myoglobinuria, 741
differentiation of, 743t
- Auditory tube diverticulum, fistulation of, 388
- Aural plaques, 212

Auriculopalpebral (motor) nerve block, 459
 Auriculopalpebral nerve block, 478
 Aurothioglucose (Solganal) for pemphigus foliaceus, 218
 Auscultation in foal pneumonia, 669
 Australia
 embryo transfers in, 277
 poisonous plants in, 426
 stringhalt in, 761
 Authorized medications in racing, 34
 Autoimmune disease, 197
 Autoimmune skin disease, 217
 Autonomous zones of innervation, 738f
 Autoregulation, failure of, 346
 Avermectin for equine pastern dermatitis, 203
 AVMA. *See* American Veterinary Medical Association (AVMA)
 Axial deviation of the aryepiglottic folds (ADAF), 378-380
 clinical signs of, 378-379
 diagnosis of, 378-379
 in exercising horse, 379f
 prognosis of, 380
 treatment of, 379-380
 Axial division of epiglottic entrapment, laser surgery of, 395
 Axillary nodular necrosis, 207
 Azithromycin, 10, 770
 for foal diarrhea, 678
 for foal pneumonia, 672
 for *Rhodococcus equi* infections, 62
 Azium. *See* Dexamethasone (Azium)
 Azium for equine recurrent uveitis, 471t
 Azotemia, 820, 847, 856

B

B4 frozen semen extender, 270
Babesia, 345
Babesia caballi, 347
Babesia equi. *See* *Theileria equi*
Bacillus Calmette Guérin (BCG), 205
 adverse effects of, 447
Bacillus cereus, 27
Bacillus clausii, 27
Bacillus licheniformis, 711
Bacillus subtilis, 711
Bacillus toyoi, 711
 Bacitracin for *Clostridium difficile* infection, 168
 Bacitracin-neomycin-bactericidal for ocular emergencies, 463t
 Back
 examination of, 495
 soreness of, 497
 Baclofen for stringhalt, 761
 Bacteremia in foals, 634, 693
 Bacteria, 6-7
 causing interstitial pneumonia, 425
 Bacterial culture for eyelid lacerations, 464
 Bacterial endocarditis, 596
 in aortic leaflets, 618
 Bacterial keratitis, 478
 Bacterial meningoencephalitis, 775
 Bacterial pathogens, drug selection for, 7t
 Bacteriostatic drugs, dosage optimization of, 9
Bacteroides, 6
Bacteroides fragilis, 6, 156
 in pleuropneumonia, 424
 Bactoderm. *See* Mupirocin ointment (Bactoderm)
 BAL. *See* Bronchoalveolar lavage (BAL)

Balanitis, 303
 Balanoposthitis, 303
 BALF. *See* Bronchoalveolar lavage fluid (BALF)
 Ballistic shock wave lithotripsy for cystic calculi, 833
 Balloon-tipped catheters to occlude retrograde flow, 390
 BALP. *See* Bone-specific alkaline phosphatase (BALP)
 Bameira, 69
 Banamine. *See* Flunixin meglumine (Banamine)
 Bandage bow, 547
 Bandage cast, 550-551, 550f
 Bandages, 547-551
 for alsike clover poisoning, 791
 for distal tarsal joint arthrodesis, 540-541
 for orthopedic patient, 544-545
 Bandaging tape, 547, 548
 9-banded armadillo (*Dasypus novemcinctus*), 69
 Barbiturates, neonatal metabolism of, 3
 Bard Parker scalpel blade, 478
 Barium enemas of foals, 683
 Barley, mineral content of, 721t
 Barotrauma, 652
 Barrel distortion optical aberration, 455
 Barrel racing, 429
 Basal energy expenditure, 112
 Basal nuclei, 764
 Base-apex electrocardiogram, 577f
 atrioventricular block
 Arab mare, 606f
 from thoroughbred on treadmill, 586f
 Base-apex lead, 576
 Bastard stranglers, 64, 65
 Bath oil sprays, 185
 Baypamun HK, 447
 BCAA. *See* Branched-chain (BCAA)
 BCG. *See* *Bacillus Calmette Guérin* (BCG)
 BCS. *See* Body condition score (BCS)
 BDP. *See* Beclomethasone dipropionate (BDP)
 Beclomethasone dipropionate (BDP)
 for heaves, 419, 420
 for recurrent airway obstruction, 442-443, 444
 Beet pulp, mineral content of, 721t
 Behavioral problems
 in stallions, 317-319
 of mares, 264-265
 Belgians
 alloantigens in, 355
 prekallikrein deficiency in, 353
 Belly band for abdominal wall hernias, 310
 Belly lift exercise, 571
 Benzalkonium, 437
 Benzimidazole
 cyathostomiasis resistance to, 162
 for gastric ulcers, 98
 for intestinal tapeworm, 159
 Benzodiazepines
 for nursing avoidance in mares, 265
 for stiff horse syndrome, 763
 Benzoyl peroxide for equine pastern dermatitis, 202
 Benzotropine mesylate for priapism, 304-305
 Bermudagrass, mineral content of, 721t
 Bernoulli equation, 579
Berteroa incana toxicosis, 787-788
 Betadine for eyelid lacerations, 465

Betamethasone
 equine studies of, 552
 for cutaneous lymphosarcoma, 210
 recommended dosage of, 553
 Bethanechol
 for cecal impaction, 140
 for EHV-1 myelitis, 754
 for EHV-1 myeloencephalitis, 752
 for gastric flow obstruction, 103
 for ileus, 109-110
 for incontinence, 825
 for perinatal asphyxia syndrome, 648, 648t
 Bicarbonate for dehydration, 119
 Big liver disease, 790
 Bilateral conjunctivitis attributable to equine herpesvirus, 474
 Bilateral hip flexion in caudal presentation, 321
 Bilateral hock flexion, 320
 Bilateral laryngeal paralysis
 causing postanesthetic upper respiratory tract obstruction, 391-392
 Bile acids, 95
 Biliary hyperplasia, 170
 Bilirubin encephalopathy, 636
 Bilirubinemia, 640
 Binocular depth perception, 455
 Bioactive proteins, 437
 Biochemical markers, 513
 Biochemical profile of peritonitis, 154
 Biochemical tests for liver disease, 169-170
 Biologic response modifiers in respiratory disease treatment, 445-448
 Biomarkers
 cartilage degradation, 514-517
 clearance from joints, 514f
 of joint disease, 513-520
 of joint tissue metabolism, 516t
 of skeletal tissue turnover, 515t
 selection of, 514
 utilization of, 513-514
 Biopsy punch, 178
 Biosecurity, 26
 Bismuth subsalicylate for foals with rotoviral diarrhea, 680
 Bit, resistance to, 570
 Bit seat, 82
 Biting flies, 570
 management of, 192b
 Biting midges, 191-192
 BIV. *See* Bovine immunodeficiency virus (BIV)
 Bivona catheter, 236
 Black beetles, 784
 Black blow fly, 194
 Black flies, 191
 Black fly dermatitis, 186
 Black hair follicle dystrophy, 219
 Black tea bag for equine pastern dermatitis, 202
 Bladder
 displacement of, 838-839
 eversion of, 326
 hypoplasia of, 827-828
 neoplasms of, 835-836
 prolapse of, 326
 rupture of, 326
 squamous cell carcinoma of, 836
 Blepharitis, 482
 Blepharospasms, 462, 478
 Blind spots, 455
 Blind staggers associated with signs of forebrain disease, 765-766

- Blindness, 773
 secondary to neurologic disease, 476
 Blink reflex, 476
 Blinking, 489
 Blister beetle. *See Epicauta* (blister beetle)
 Blister beetles
 control of, 786
 toxicosis, 779, 784-786
 Blood
 administration of, 356
 biomarker sampling, 514
 Blood ammonia, measurement of, 170
 Blood aqueous barrier, permeability of, 461
 Blood components therapy, 356
 alternatives to, 356
 Blood flow, relative, 503
 Blood gas analysis for foal pneumonia, 679
 Blood loss, 340-341
 Blood loss anemia, diagnosis of, 337, 340-341
 Blood samples for drug testing, 32
 Blood tests for cranial nerve diseases, 776
 Blood typing for embryo transfers, 277
 Blood urea nitrogen (BUN), 820
 Blood volume of neonatal foal, 640
 Blood-brain barrier in foals, 688
 Blunt head trauma
 causing optic nerve damage, 467
 globe proptosis, 464
 Blunt ocular trauma, 467
 Blunt trauma
 global rupture, 464
 to penile shaft, 303
 Body, condition of in cardiovascular examination, 573
 Body condition score (BCS), 698, 706
 Body fluids, biomarker sampling, 514
 Body temperature
 and retained fetal membranes, 331
 of premature foals, 643
 Bolz technique, 304
 Bone degradation markers, 517-518
 Bone density, computed tomography, 507
 Bone, edema of, magnetic resonance imaging of, 509
 Bone marrow aplasia, anemia due to, 343
 Bone marrow aspirate, 339
 Bone phase of musculoskeletal nuclear scintigraphy, 500
 Bone sialoprotein (BSP), 518
 Bone spavin, 496
 Bone synthesis markers, 518
 Bone-specific alkaline phosphatase (BALP), 518
 Bony column, insufficient support of, 535
Boophilus microplus, 189
Bordetella bronchiseptica in foal pneumonia, 666
 Boric acid wipes for equine pastern dermatitis, 202
Borrelia burgdorferi, 54, 775
 enzootic cycle of, 55f
 Botulinum antitoxin, 745
 Botulism, 735, 740, 775, 799-801
 clinical signs of, 799-800
 diagnosis of, 744, 800
 differentiation of, 743t
 etiology of, 799
 immunization for, 357
 pathogenesis of, 799
 prevention of, 800
 prognosis of, 800
 Botulism—cont'd
 treatment of, 800
 vaccine for, 252
 Bovine colostrum, 694
 Bovine immunodeficiency virus (BIV), 45
 Bovine papillomavirus, 204
 Bovine respiratory syncytial virus (BRSV), 674
 Bowel mucosa, barrier function of, 114
 Brachiocephalicus, pain in, 495
 Brachygnathia, 86, 86f
 Brachytherapy for squamous cell carcinoma, 483
 Bradydysrhythmias, 573
 Brain abscess, 766
 Brain disease, signs of, 70-71
 Brain tumors, 766-767
 computed tomography of, 507
 Brainstem, 772
 toxicity, 775
 Brainstem disease
 causes of, 773-774
 treatment of, 777-778
 Bran mash for rectal tears, 152
 Branched-chain (BCAA) to aromatic amino acids, 718
 Brans, mineral content of, 721t
 Brazil, embryo transfers in, 277
 Breakover, 497
 Breathing in cardiopulmonary resuscitation of newborn foal, 652
 Breech posture, 320
 Breech presentation, 321
 Breed registry guidelines for donor mares, 277
 Breeding
 care of after, 250
 commercial, 248-250
 per conception, 248
 Breeding mares
 chromosomal abnormalities in, 261
 gonadal hypoplasia in, 261
 postpartum hemorrhage in, 327
 selection of, 248-249, 272
 time determination for, 249-250
 Breeding soundness examination (BSE), 253
 for artificial insemination, 272
 for embryo transfers, 277
 for recipient mares, 278-269
 Breeding stallion, clinical problems in, 303-309
 Breeding stitches, 303
 Bretylium
 for dysrhythmias, 604t
 for ventricular fibrillation, 612-613
 Bretylium tosylate for cardiopulmonary resuscitation of newborn foal, 654
 Bricanyl. *See* Terbutaline sulfate (Bricanyl)
 Bridging techniques for valgus and varus deviations, 665
 Broad ligament
 hematoma of, 328
 effect on peritoneal fluid, 296
 Broken wind, 793
 Bromhexine hydrochloride for foal pneumonia, 672
 Bromosulphophthalein test, 170
 Bronchiointerstitial pneumonia, 425
 Bronchiolitis and exercise intolerance, 413
 Bronchitis
 and exercise intolerance, 413
 chronic
 definition of, 412
 Bronchoalveolar lavage (BAL), 407-411, 416, 794
 cytology of, 409t
 with respiratory disease, 410t
 for exercise-induced pulmonary hemorrhage, 429
 for inflammatory airway disease, 416
 from athletic horse, 409f
 indications for, 407-408
 inflammation in, 413
 inflammatory cells in
 normal range of, 416
 procedure for, 408
 vs. tracheal aspirate, 401-402
 Bronchoalveolar lavage fluid (BALF), 446
 Bronchoconstriction, viral infection in, 414
 Bronchodilators, 437
 aerosolized, 440-445
 for foal pneumonia, 673
 for heaves, 419
 for interstitial pneumonia, 428
 Bronchoesophagoscopic forceps, 379, 380f
 Bronchiointerstitial pneumonia, 674-676
 Bronchopneumonia, 425
 Bronchospasm, 442
 Bronze blow flies, 194
 Broodmares. *See also* Breeding mares
 postpartum hemorrhage in, 327
 selection of, 272
 BRSV. *See* Bovine respiratory syncytial virus (BRSV)
 Brucellosis, 469
 BSE. *See* Breeding soundness examination (BSE)
 BSP. *See* Bone sialoprotein (BSP)
 Buckthorn, 784
 Bulk pelleted feed, 723
 Bullae, 217
 Bullous pemphigoid, 89
 Bullous stomatitis, 89
 BUN. *See* Blood urea nitrogen (BUN)
 Bunny hopping gaits, 756, 760
 Buphthalmos, 487
 Burns, 540
 classification of, 220-221
 clinical protocol for, 223t
 complications of, 224
 healing of, 221, 224
 iatrogenic, 222
 management of, 220-225
 prognosis of, 224-225
 Burns, Pat, 270
 Burrow weed, 783
 Buscopan for large colon impaction, 133
 Buserelin inducing ovulation, 273
 Butorphanol, 260, 286
 for cecal impaction, 140
 for colic, 117
 for foals, 691
 for ocular emergencies, 463t, 464t
 for permanent tracheostomy in standing horses, 397
 for small intestine strangulating obstruction, 124
 for stranglers, 67
 in critical care, 20
C
 Cache Valley virus, 766
 Caddisfly (*Dicosmoecus gilvipes*), 75
 CAEV. *See* Caprine arthritis-encephalitis virus (CAEV)
 Caffeine clearance test, 170

- Caffeine for perinatal asphyxia syndrome, 648t, 649
- Calcium
and readiness for birth, 315, 316
for cardiopulmonary resuscitation of newborn foal, 654
in feed, 721t
- Calcium alginate dressing for thermal burns, 222-223
- Calcium borogluconate for dehydration, 156
- Calcium carbonate calculi, formation of, 719
- Calcium carbonate for gastric ulcers, 96
- Calcium gluconate for myasthenia, 745
- Calcium pentosan polysulfate (CaPPS), 557
- Calciiviruses, 52, 88
- California encephalitis, 766
- Calories, requirements for, 112
- Calvaria fractures, computed tomography of, 507
- Campylobacter* in foal diarrhea, 679
- Campylobacter jejuni* causing weanling diarrhea, 165
- Candida*, 477, 792
causing placentitis, 297
- Canine teeth, 85
- Cantharidin, 52, 89
intoxication, 784
mechanisms of action, 785
toxicosis, 785-786
- Capillary refill time, 573
in peritonitis, 154
- Capnograph in cardiopulmonary resuscitation of foals, 654
- CaPPS. *See* Calcium pentosan polysulfate (CaPPS)
- Caprine arthritis-encephalitis virus (CAEV), 45
- Caprine Serum Fraction
Immunomodulator (CSFI), 447-448
- Capsular rotation, alternative methods of shoeing, 525-528
- Captan for folliculitis, 200
- Carafate. *See* Sucralfate (Carafate)
- Carbamate, 786
for mite control, 190
- Carbaryl for mite control, 190
- Carbocaine for foals, 691
- Carbohydrates
as energy source, 112
public health effects of, 701
- Carbon dioxide laser, 394
for squamous cell carcinoma, 484
- Carbonic anhydrase inhibitors for glaucoma, 487
- Cardiac auscultation, 574-575
- Cardiac cachexia, 573
- Cardiac catheterization, 584-585, 589-591
- Cardiac development, 591-592
- Cardiac enzymes, 611
- Cardiac glycoside-containing plants, 783
- Cardiac impulse, palpation of, 575
- Cardiac isoenzymes, 588-589
in acquired pericardial disease, 622
in myocardial disease, 620-621
- Cardiac morphogenesis, 591-592
- Cardiac murmurs. *See* Murmurs
- Cardiac tamponade, 622
- Cardiac troponin-I (cTNI), 588-589
in myocardial disease, 620
- Cardiogenic edema, 573
- Cardiopulmonary resuscitation
of newborn foal, 650-655
care of foals after, 654-655
cessation of, 654
equipment for, 650-651
monitoring of, 654
ordered plan for, 651-654
- Cardiovascular disease, laboratory tests for, 584
- Cardiovascular examination, 572-584
clinical, 573-574
historical findings in, 572-573
signalment, 573
- Cardiovascular function in performance
horse, evaluation of, 585-591
- Cardiovascular system, diagnostic aids for, 576-577
- Carnitine, 28
- Carotid arteries, occlusions of, 376
- Carpal joint
disease of in sport horses, 498
distention of
evaluation of, 496
passive range of motion of, 545f
- Carprofen (Rimadyl)
for colic, 117
for joint disease, 560
for neonates, 5
- Carprofen (Zenecarp), 12-13
- Carpus
computed tomography of, 506
flexion of, 497
radiography of, 498
- Carrot stretches, 568
- Cartilage
degradation of
biomarkers, 514-517
synthesis markers, 517-518
- Cartilage oligomeric matrix protein (COMP), 517, 519
- Caruncle, 452
- Cascabela thevetioides*, 783
- Caslick procedure, 323, 333
- Caslick's stitches, 303
- Cassia, 782
- Casting tape, 550
- Castration for testicular torsion, 309
- Casts, 548-551, 821
application of, 549
- Cataplasms, 16
- Cataract surgery, 457
- Cataracts, 466-467, 472
cause of, 467
- Catheter EMAC800, 402
- Catheter V-EBAL-8.0-190, 402
- Cattle grubs, 194
- Cauda equina, 755
damage to
clinical signs of, 755
diagnosis of, 758-759
traumatic damage to, 755-756
- Cauda equina neuritis, 735, 739
- Cauda equina syndrome, 755
treatment of, 759-760
- Caudal bulla, 369
- Caudal heel pain, 500, 532-535
bony column support, 535
digital flexor apparatus
contracture of, 534-535
long breakover, 532-535
- Caudal hooks, 84f
- Caudal maxillary sinus, portals for, 372
- Caudal presentation, 321
- Caudal wither region, pain in, 571
- Caustic burns, 220, 221
- Cavitation, definition of, 564f
- Cavitation effect, 564f
- Cayenne, 570
- CBC. *See* Complete blood count (CBC)
- CD14. *See* Cluster differentiation antigen 14 (CD14)
- Cecocolic intussusceptions, 149
- Cecocolic intussusceptions, 149
- Cecum
anatomy and physiology of, 138
decompression of, 115
distention of, 702
impaction of, 138-141
clinical signs of, 139
diagnosis of, 139
pathogenesis of, 138-139
prognosis of, 140-141
surgery of, 140
treatment of, 139-140
motility patterns of, 138
- Cefadroxil, 10
oral administration of, 7
- Cefazolin, 10
for neonatal septicemia, 3
- Cefepime (Maxipime), 7, 11
for neonatal septicemia, 4
- Cefotaxime, 7
for neonatal septicemia, 4, 661t
- Cefotetan, 6
- Cefoxitin, 6
- Ceftazidime, 7
for neonatal septicemia, 4
- Ceftiofur (Naxcel), 10
for cystitis, 838
for duodenitis-proximal jejunitis, 123
for foal pneumonia, 671
for neonatal septicemia, 4, 661t
for perinatal asphyxia syndrome, 648t
for peritonitis, 156
for pregnant mares, 231
for respiratory disease, 39
for strangles, 66
- Ceftriaxone, 10
- Celestone Soluspan, 552
- Celiotomy, 723
- Cell membranes, lipoperoxidation of, 136
- Cell wall extract of *Mycobacterium bovis*, 446-447
- Cellulitis, prevention of, 304
- Cellulose, 698
- Cenataurea solstitialis*, 780
- Centesis of nasal passage, 371-372
- CEPEF. *See* Confidential Enquiry into Perioperative Fatalities (CEPEF)
- Cephalosporins, 10-11
for choledocholithiasis, 172
for duodenitis-proximal jejunitis, 123
for foal diarrhea, 679
for neonatal septicemia, 3
oral administration of, 7
- Cephalosporium*, 792
- Cephapirin, 10
- Cereals, recommendations for, 703
- Cerebral cortex, 764
- Cerebral fluid analysis for equine protozoal myeloencephalitis, 72
- Cerebrocortical edema, therapy of, 770t
- Cerebrospinal fluid, analysis of
in cauda equina damage, 759
in cranial nerve diseases, 776-777
in forebrain disease, 768-769
- Cervical cord disease, cause of, 749-750
- Cervical dilation prior to parturition
induction, 316
- Cervical myelography, 748

- Cervical spinal cord disease
ataxia associated with, 746-750
clinical signs of, 746-747
Cervical star, 297
Cervical stenotic myelopathy, 747-748
Cervix
examination of
for embryo transfers, 277
in after foaling mare, 249
lacerations of, 334-335
manual examination of, 334
Cesarean section, 322
for abdominal wall hernias, 310
Cestrum diurnum, 784
Charcoal for ionophore toxicity, 745
Chasteberry, 811
Cheek teeth malocclusions, 82-85
Chemical ablation for progressive
ethmoid hematoma, 377-378
Chemical burns, treatment of, 223, 466
Chemical injuries to cornea, 466
Chemical restraining agents in
thermography, 503-504
Chemical restraints during artificial
insemination, 273
Chemicals affecting spermatozoa, 266
Chemistry analyzer, mammary secretion
electrolytes, 315-316
Chemosis, 462, 465
Chemotherapy
for cutaneous lymphosarcoma, 211
for sarcoid, 485
Chest radiography of exercise-induced
pulmonary hemorrhage, 431
Chest tube, drainage of pleural fluid in
pleuropneumonia, 423f
Cheyletus eruditus, 189
Chiggers, 188
Chiropractic, 567-568
Chloral hydrate for colic, 117
Chlorambucil (Leukeran)
for cutaneous lymphosarcoma, 211
for lymphoma, 361
Chloramphenicol, 6, 770
dosage optimization of, 9
for foal pneumonia, 671
for foals, 688
for neonatal septicemia, 4
for neonates, 4
for ocular emergencies, 463t
for pleuropneumonia, 424
for proliferative enteropathy, 165
neonatal absorption of, 1
neonatal metabolism of, 3
Chlorbutol, 437
Chlorhexidine, 25
for equine pastern dermatitis, 202
for folliculitis, 200
Chlorhexidine shampoo, 199
for staphylococcal bacterial folliculitis,
198
Chlorhexidine solution for thermal
burns, 222
Chlorofluorocarbon propellant for
metered drug delivery, 437
Chlorpheniramine
for arthropod hypersensitivity, 185
for atopic dermatitis, 183
Chlortetracycline for proliferative
enteropathy, 165
Cholangiohepatitis, 170
acute, 170
treatment of, 172
Cholelithiasis, 172
Cholesteatomas, 767
Cholestyramine for *Clostridium difficile*
infection, 168
Chondroids, 65
removal of, 387
Chondroitin sulfate, 557, 570
for cartilage degradation, 515, 517
Chondroprotective therapy, 26
Chorioptes bovis, 187, 201
Chorioptes equi, 176, 187
Chorioptes mites, 190
Chorioretinal degeneration, 467
Chorioretinitis, 476
Chorulon
for recipient mares, 279
ovulation induction, 278
Chromium, 28
for ECD, 717
for exertional rhabdomyolysis, 730
supplementation, 811
Chromophores, 174
Chromosomal abnormalities in breeding
mares, 261
Chronic blood loss, 341-342
Chronic bronchitis, definition of, 412
Chronic exertional rhabdomyolysis, 727-
728
diagnosis of, 728-729
feeding recommendations for, 731t
Chronic laminitis, 520-528
medical treatment of, 526
nutritional management of, 526
pathophysiology of, 520-521
surgical treatment of, 526-528
treatment failure, 528
Chronic muscle pain, 569
Chronic nonsuppurative inflammatory
hepatitis, 172-173
Chronic obstructive pulmonary disease
(COPD), 417-421, 793-794
definition of, 412
Chronic renal failure, 845-848
clinical signs of, 845-846
diagnosis of, 846-847
etiology of, 845
prognosis of, 848
treatment of, 847-848
Chronic selenosis
clinical signs of, 802-803
front hoof in, 803f
Chronic wasting, 790
Chrysops, 186, 191
Ciliated columnar endometrial cells,
227f
Cimetidine (Tagamet)
for gastric ulcers, 98
for neonatal gastric ulcers, 5
for perinatal asphyxia syndrome, 648t
Ciprofloxacin, 10
for ocular emergencies, 463t
Circling in cranial nerve diseases, 772
Circulation in cardiopulmonary
resuscitation of newborn foal,
652-653
Circulatory collapse, 355
Circulatory pattern, 503
Cisapride
for cecal impaction, 140
for perinatal asphyxia syndrome, 648,
648t
Cisplatin for equine sarcoid, 205
CK-MB, 611. *See* Creatine kinase (CK)
Cladosporium, 477
Clarithromycin, 10
for foal pneumonia, 672
for *Rhodococcus equi* infections, 62
Classic equine recurrent uveitis (ERU),
468-469
Claviceps purpurea, 796
Cleaning, 25
Cleaved type I collagen, 518
Cleaved type II collagen, 516
Clenbuterol (Ventipulmin)
for anhidrosis, 817-818
for exercise-induced pulmonary
hemorrhage, 433
for fetal compromise, 632
for foal pneumonia, 673
for heaves, 419, 420
for placental hydrops, 302
for placentitis, 300
Clenbuterol-MBA derivative, 34f
Client education
for penile hygiene, 836
for recurrent airway obstruction, 441
Climate and tapeworm infection, 158
Clindamycin, 6
dosage optimization of, 9
Clitoris, hypertrophy of with granulosa
cell tumors, 262
Cloprostenol
for abdominal wall hernias, 310
for persistent mating-induced
endometritis, 236
for placental hydrops, 301
Closed pneumothorax, 434
Clostridia, 6
causing intravascular hemolysis, 345
causing weanling diarrhea, 165
complicating burns, 224
Clostridium botulinum, 740, 744, 799
Clostridium chauvoei, 620
Clostridium difficile, 58, 62, 167, 678, 711
Clostridium difficile infection, 166-169
clinical manifestations of, 166-167
clinical signs of, 167
diagnosis of, 167-168
in neonatal foals, 167
prevention of, 169
treatment of, 168
Clostridium perfringens, 58
causing enteritis, 167
with foal diarrhea, 678
Clotrimazole
for guttural pouch mycosis, 389
for uterine infection, 231
Clover-associated photosensitization, 779
Cluster differentiation antigen 14
(CD14), 104
Clydesdale horse, visual perspective of,
455
Coagulation disorders
acquired, 353-354
inherited, 351
Coagulopathy causing blood loss, 336
Coastal Bermuda grass hay, fiber in, 127
Cobalt deficiency, 342
Coccidioides, 374, 792
Cochliomyia macelaria, 194
Coenzyme Q10, 28-29
Coffee senna, 782
Coffee weed, 782
Coffin bone, cystic lesions in, computed
tomography of, 506
Coffin joint injection, 556
Coggins test, 46
for equine infectious anemia, 347
Coital exanthema, 88
Colchicine for chronic nonsuppurative
inflammatory hepatitis, 173
Cold running water for thermal burns, 222

- Cold water hydrotherapy
for hydroceles, 307
for penile trauma, 303
- Cold water therapy for peripheral nerve disease, 739
- Colic, 57, 784
and tapeworm infection, 158
causing angular limb deformities, 663
dehydration with, 115-120
display of, 132
flunixin meglumine for, 559
in foals, 680-686
abdominal radiography of, 683-684
abdominal ultrasonography of, 682-683
duodenoscopy, 685
gastrosocopy, 685
history of, 681
nasogastric intubation, 682
peritoneal fluid analysis, 684-685
physical examination of, 681-682
signalment, 680-681
surgical decision making, 686
treatment of, 685-686
in postfoaling mare, 328
management of, 99-100
monitoring for, 710
pain with, 115-120
parenteral nutrition for, 111-115
with testicular torsion, 309
- Colitis
in septic foals, 657
nutritional therapy of, 723-724
- Collagen assays
for cartilage degradation, 516-517, 518
for bone synthesis, 518
for cartilage synthesis, 517
- Collagen crosslinks, 517, 518
- Collagen degeneration, 206-207
- Collagenolytic granuloma, 206-207
- Collateral cartilages, ossification of, 498
- Collateral ligaments of distal interphalangeal joint, 532
- Colloidal therapy
for acute blood loss, 341
for salmonellosis, 59
- Colloids
for *Clostridium difficile* infection, 168
for dehydration, 119
- Colon
decompression of, 115
tympany of, 132
- Colonic atresia, 681
- Colonic sand impaction
of foal
abdominal radiograph of, 684f
- Colonic volvulus
diagnosis of, 150
- Color flow Doppler, 579
for aortic aneurysms, 624
for aortic regurgitation, 618
for aortocardiac fistulas, 625
for tricuspid regurgitation, 613
jugular vein thrombophlebitis, 626
of mitral valve, 616
of regurgitant jet, 617
- Color vision, 457
- Colostomy, complications of, 153
- Colostrum immunity, 692-693
- Colostrum, 324
and readiness for birth, 315
failure to absorb, 693
failure to ingest adequate volume of, 693
for perinatal asphyxia syndrome, 648t
- Colostrum—cont'd
inadequate immunoglobulin content in, 693
loss of, 632, 693
- Combination chemotherapy for cutaneous lymphosarcoma, 211
- Comet-tail artifacts, 421
- Commercial horse breeding, 248-250
- Commercial lipid emulsions in parenteral nutrition, 112-113
- Commercial probiotics, 712-713
- Common atrioventricular valve, malformed, 592f
- Common ventricle, 599
- COMP. *See* Cartilage oligomeric matrix protein (COMP)
- Compatibility testing, 355
- Competing horses, intraarticular corticosteroids for, regulatory issues associated with, 554
- Complement fixation tests, 52
- Complement in colostrum, 692
- Complementary therapy
clinical indications for, 568b
for musculoskeletal disorders, 567-571
indications for, 570-571
- Complete blood count (CBC), 820
for foal pneumonia, 669
for peritonitis, 154
for *Rhodococcus equi* infections, 61
with cauda equina damage, 758
- Compulsive salt/glucose consumption, 831
- Computed tomography
clinical indications for, 506
clinical uses of, 505-507
for cervical stenotic myelopathy, 748
of nasal passages, 371
- Conception
breeding per, 248
rate of, 248
- Conduction, 503
- Confidential Enquiry into Perioperative Fatalities (CEPEF), 687
- Conformation, prepurchase examination, 493-495
- Conformational sheared heels, 529
- Congenital diaphragmatic hernia, 435
- Congenital disorders of urinary tract, 826-827
- Congenital heart disease, 591-601
clinical signs of, 594-596, 595f
diagnosis of, 594-596
etiology of, 593-594
prevalence of, 593-594
- Congenital papillomas, 212
- Congenital skin disease, 219
- Congestive heart failure, 574
atrial fibrillation with, 609-610
signs of, 614-615
treatment of, 617
two-dimensional echocardiography, 615f
- Conjugated estrogens (Primarin) in critical care, 21
- Conjunctiva
examination of, 452
hemorrhage of, 465
hyperemia of, 462
lacerations of, 464-465
slit lamp biomicroscope examination of, 450
- Conjunctival flap for corneal ulcers, 466
- Conjunctival hyperemia, 474
- Conjunctivitis, clinical signs of, 473-474
- Conserved forages, 701
- Contact dermatitis, histopathology of, 179
- Contact reactions, 178
- Continuous ambulatory electrocardiography, 602
for atrial fibrillation, 608
for ventricular ectopy, 610-611
- Continuous murmurs, echocardiogram indications for, 614b
- Continuous passive motion (CPM), 545
- Continuous-wave Doppler, 579
for aortic regurgitation, 619f
- Contra coup force, 467
- Contrast arteriography for guttural pouch mycosis, 390
- Contrast echocardiography, 579-580
- Contrast radiography for esophageal obstruction, 91-92, 92f
- Contrast sensitivity, 455
- Contrast studies of foals, 683
- Conus arteriosus, 592
- Conus medullaris, 755
- Convallaria majalis*, 783
- Convection, 503
- Cool water hydrotherapy for *berteroa incana* toxicosis, 788
- Cooled semen
for artificial insemination
dosage of, 275
vs. cryopreserved semen
fertility rates of, 274
- Cooled-transported semen program, 241
- Coombs' test, 346
for immune-mediated hemolytic anemia, 360
- COPD. *See* Chronic obstructive pulmonary disease (COPD)
- Copper
deficiency of, 342, 620
for cervical stenotic myelopathy, 748
- Copperhead (*Agkistrodon* spp.) causing intravascular hemolysis, 345
- Cor pulmonale, 428
- Core hay sampling devices, 706
- Core vitrectomy, 472t
for equine recurrent uveitis, 470-472
- Corn, 99
mineral content of, 721t
providing calories, 718
supplements of
for colitis, 724
- Corn oil, 724
for right dorsal colitis, 142
- Cornea
abscess of, 466
burns of, 466
damage to, 224
deep abscesses of, 461
degeneration of, 478
direct ophthalmoscopy of, 451
dystrophy of, 478
edema of, 467, 478
emergency treatment of, 465-466
epithelial integrity of, 462
examination of, 453
lacerations of, 465
neovascularization, 478
opacity of, 450
penetrability of by topical ocular drugs, 458b
perforation of, 464
reflection, 453
reflexes, 451
sensitivity of, 476

- Cornea—cont'd
stromal abscess of, 478
ulcers of, 466
 complications of, 466
 detection of, 451
 in neonates, 661
wounds of
 leakage of, 451
- Corneas
stromal abscess of, 466
treatment of, 479
- Corners navicular disease affecting, 498
- Coronary band grooving, 527-528
- Coronavirus, 680
causing enteritis, 167
- Corpora nigra, 453, 454-455
- Corpus hemorrhagicum, 261
- Corpus luteum, regression of, 249
- Corticosteroids
and immunopathology tests, 218
antiinflammatory effect of, 442
contraindications for, 465
exacerbating herpesvirus
 keratoconjunctivitis, 475
for acquired pericardial disease, 623
for atopic dermatitis, 182-183
for chronic nonsuppurative
 inflammatory hepatitis, 172-173
for cutaneous lymphosarcoma, 210
for disseminated intravascular
 coagulation, 353-354
for dysrhythmias, 605
for EMND, 745
for endotoxemia, 107
for equine herpesvirus
 myeloencephalopathy, 40
for equine influenza, 43
for equine recurrent uveitis, 470
for fibrocartilaginous emboli, 753
for forebrain disease, 770
for glaucoma, 487
for heaves, 418
for herpetic keratitis, 476
for hypersensitivity, 193
for idiopathic eosinophilic
 enterocolitis, 147
for immune-mediated hemolytic
 anemia, 346
for multisystemic eosinophilic
 epitheliotropic disease, 147
for myocardial disease, 621
for peripheral nerve disease, 739
for premature foals, 644
for sick neonatal foals, 640
for spinal cord trauma, 749
for upper airway disease, 399
for urticaria, 206
in critical care, 20
interfering with skin test results, 182
postinjection exercise protocol, 553
side effects of, 419
subconjunctival injection of, 459
with sodium hyaluronate, 553
- Corynebacterium*, 213, 838
- Corynebacterium parvum*, 446
- Cost
of donor mares, 277
of exogenous thyroid hormone
 supplementation, 251
of parenteral nutrition, 113
of thyroid hormone assays, 251
- Cottonmouth (*Agkistrodon piscivorus*)
causing intravascular hemolysis, 345
- Coughing, 401
in foal pneumonia, 668
in inflammatory airway disease, 413
in non-racehorses
 inflammatory airway disease
 diagnosis in, 416
in racehorses
 diagnostic approach to, 415
- Coumaphos
for equine pastern dermatitis, 203
for mite control, 190
- COX-1. *See* Cyclooxygenase-1 (COX-1)
- COX-2. *See* Cyclooxygenase-2 (COX-2)
- Coyotillo, 784
- CPIII. *See* C-propeptide (CPIII)
- CPM. *See* Continuous passive motion (CPM)
- C-propeptide (CPIII), 517
- Crabbing, 70
- Cracked heels, 201-203
- Cranial (anterior) presentation, 321
- Cranial mediastinum, melanoma of,
 sonographic appearance of, 424f
- Cranial mesenteric artery,
 thromboembolism of, 626
- Cranial nerve diseases, 772-777
clinical signs of, 772-773
diagnosis of, 776-777
- Cranial thoracic pain, 496
- Craniotomy, 770
- Creatine, 28
- Creatine kinase (CK), 588-589, 620, 744, 762
- Crested neck with granulosa cell tumors, 262
- Cresty neck, 814
- Cricothyroideus dorsalis, atrophy of, 383
- Critical care therapeutics, 19-23
- Crocodile clips, 576
- Crofton weed (*Eupatorium adenophorum*), 426
- Crohn's disease, 146
- Cross-galloping in prepurchase
 examination, 497
- Cross-matching, 355
- Crotalaria*, 426, 768, 788, 789
- Crotalus* spp. *See* Rattlesnakes (*Crotalus* spp.)
- Crown, displaced fragments of, 374
- Crude protein requirements, equations
for, 723b
- Cryogen, 377
- Cryogenic ablation of progressive
 ethmoid hematoma, 377
- Cryoprecipitate, 356
- Cryopreserved semen, 269-271, 282-283
vs. cooled semen
 fertility rates of, 274
- Cryoprotectants, 282
- Cryosurgery for sarcoid, 485
- Cryotherapy for squamous cell
 carcinoma, 483-484
- Cryptococcus*, 374
causing interstitial pneumonia, 426
- Cryptococcus neoformans*, 758
- Cryptosporidia, causing enteritis, 167
- Cryptosporidial enteritis of foals, 697
- Cryptosporidium* with foal diarrhea, 678
- Crystalloids
for acute blood loss, 341
for ascending colon volvulus, 137
- CSFI. *See* Caprine Serum Fraction Immunomodulator (CSFI)
- C-telopeptide crosslink (CTX) assay, 518
- CTn1, 611
- CTNI. *See* Cardiac troponin-I (cTNI)
- CTX assay. *See* C-telopeptide crosslink (CTX) assay
- Cuboidal bones, incomplete ossification
of, 664
- Cuboidal cells, 228
- Culex tarsalis*, 48
- Culicoides*, 184, 191
- Culicoides* hypersensitivity, 184-185, 193
- Culicoides variipennis*, 184
- Culturette, 229
- Cumulus oocyte complexes, 286
- Cunean tenectomy, 541
- Curschmann's spirals, 410
- Cushing's disease, 261, 807, 829, 831
- Cushing's syndrome, 526
- Cutaneous adverse drug reactions (ADR), 177-180
histopathology of, 178-179
incidence of, 179, 180t
management of, 179-180
- Cutaneous amyloidosis, 208
- Cutaneous habronemiasis, 195-197
clinical signs of, 195-196
diagnosis of, 196
etiology of, 195
of penis, 305
pathogenesis of, 195
surgical excision of, 196
treatment of, 196-197
- Cutaneous lymphosarcoma, 209-211
clinical signs of, 209
clinicopathologic of, 209-210
diagnosis of, 210
etiology of, 209
treatment of, 210-211
- Cutaneous points relating to painful
joints, 495
- Cutaneous T cell lymphoma, 209
- Cutaneous wound, dehiscence of,
 complicating surgical ablation of
 progressive ethmoid hematoma, 377
- Cutting horses, carpal joint disease in, 498
- Cyanamide. *See* Aminophylline (Cyanamide)
- Cyanosis, 599
- Cyathostomes, 161
- Cycling mare, lymphocytes in, 228
- Cyclooxygenase (COX), 11
- Cyclooxygenase-1 (COX-1), 11, 558
- Cyclooxygenase-2 (COX-2), 11, 558
- Cyclooxygenase-2 (COX-2) inhibitors vs.
 nonselective inhibitors, 107
- Cyclopegics. *See* Mydriatic/cyclopegics
- Cyclophosphamide (Cytotoxin)
for cutaneous lymphosarcoma, 211
for lymphoma, 361
for plasma cell myeloma, 362
- Cyclophotoablation for glaucoma, 487
- Cyclosporine A
for equine recurrent uveitis, 471t
for keratitis, 476
- Cyklokapron. *See* Tranexamic acid (Cyklokapron)
- Cymodothea trifolii*, 790
- Cynoglossum*, 768, 788, 789
- Cynoglossum officinale*, 789
- Cypionate for incontinence, 825
- Cyproheptadine, 810
for Cushing's syndrome, 526
- Cystadenomas of ovaries, 262
- Cysteinyl leukotrienes, 420
- Cystic calculi, 833-834

- Cystitis, 837-838
hematuria, 854
Cystorelin, 258-259
Cystoscopy of upper urinary tract
infections, 838
Cysts, laser surgery of, 395
Cyto reduction for equine sarcoid, 205
Cytosar-U. *See* Cytosine arabinoside (Cytosar-U)
Cytosine arabinoside (Cytosar-U)
for cutaneous lymphosarcoma, 211
for lymphoma, 361
for myeloid leukemias, 362
Cytotec. *See* Synthetic prostaglandin E2 (Cytotec)
Cytotoxan. *See* Cyclophosphamide (Cytotoxan)
- D**
Dacryocystitis, 490
Daily energy expenditure, 112
Dasypus novemcinctus. *See* 9-banded armadillo (*Dasypus novemcinctus*)
Day, artificially lengthening, 237
Day-blooming jessamine, 784
DCAB. *See* Dietary cation-anion balance (DCAB)
DDAVP. *See* Desmopressin acetate (DDAVP)
DDFT. *See* Deep digital flexor tendon (DDFT)
Death, leading cause of, 135
Debridement, 423
for alsike clover poisoning, 791
for eyelid lacerations, 465
Debris in tracheal aspirates, 405-406
Deca-Durabolin. *See* Nandrolone decanoate (Deca-Durabolin)
Deciduous incisors, 86
Decompression for colic, 115
Deep digital flexor tendon (DDFT), 532
attachment of, computed tomography of, 506
obesity, 814
Deep digital flexor tenotomy, 526-527
Deep sedation for lavage tubing
installation, 459
Deer, 54
Deer flies, 46, 184, 186, 191
Deer tick (*Ixodes scapularis*), 78
Dehydration
assessment of, 118t
correction of, 156
determination of, 657
in septic peritonitis, 157
of large colon, 131
physical signs of, 125t
with colic, management of, 117-119
Delayed gastric emptying, 101
Deltasone. *See* Prednisone (Deltasone)
Dembrexine (Sputolysin) for heaves, 420
Demeanor, change in with inflammatory airway disease, 416
Demecarium bromide (Humorsol) for glaucoma, 487
Demodex, 197
Demodex caballi, 189
Demodex mites, 189
Demodicosis, 188-189
Demodicosis, skin scrapings of, 190
Denatured cartilage, 516
Dental disease, diagnosis of, 373-374
Dental examinations for breeding stallions, 252
Dental infections, signs of on lateral films, 374
Dental malocclusions
power instruments for, 81-87
dental examination for, 82
selection of, 81-82
Dental origin cysts, computed tomography of, 507
Deoxy pyridinoline, 517
Deoxyribonucleic acid-dependent protein kinase (DNA-PK), 696
Depo-Medrol. *See* Methylprednisolone acetate (Depo-Medrol)
Depth perception, 455-456
Derm Caps for atopic dermatitis, 183
Dermacentor, 347
Dermacentor andersoni, 740
Dermacentor (Anocentor) nitens, 189
Dermanyssus gallinae, 189
Dermatophilosis, 198-199
Dermatophilus, 197
Dermatophilus congolensis, 176, 198, 201
Dermatophytes, 197
Dermatophytosis, 199-200, 201
Descemet's membrane, 477
Desfuroylceftiofur, 10
Deslorelin acetate (Ovuplant)
for oocyte transfer, 285-286
for ovulation induction, 241, 273, 278
Desmopressin acetate (DDAVP), 822
for von Willebrand's disease, 352
Desmopressin response test, 830
Desmotomy for upward fixation of the patella, 537
Desoxycholate agar, 229
Detomidine hydrochloride (Dromosedan), 17, 260, 287
detection of, 32
for colic, 117
for esophageal obstruction, 93
for foals, 688-689
for forebrain disease, 769
for large colon impaction, 133
for neonatal sedation, 5
for ocular emergencies, 463t, 464t
for peritonitis, 156
for permanent tracheostomy in standing horses, 397
for rowdy breeding behavior, 318
Developmental orthopaedic disease, 518
Devil's claw, 570
Dew poisoning, 201-203, 790
Deworming for breeding stallions, 252
Dexamethasone (Azium), 67
for acute respiratory distress syndrome, 676
for arytenoid chondrosis, 382
for atopic dermatitis, 183
for cerebrocortical edema, 770t
for chronic nonsuppurative inflammatory hepatitis, 173
for cutaneous habronemiasis, 196
for cutaneous lymphosarcoma, 210
for EHV-1 myeloencephalitis, 752
for equine recurrent uveitis, 471t
for heaves, 418
for hypersensitivity, 186
for immune-mediated hemolytic anemia, 346
for lymphoma, 361
for negative-pressure pulmonary edema, 393
for ocular emergencies, 464, 464t
for orthopedic pain, 544
for oxidative erythrocyte damage, 344
for peripheral nerve disease, 739
for sterile nodular panniculitis, 208
Dexamethasone (Azium)—cont'd
for thrombocytopenia, 350
for upper airway disease, 399
for upper respiratory tract postoperative management, 395
for urticaria, 206
for vasculitis, 365
interfering with skin test results, 182
Dexamethasone suppression test with pituitary pars intermedia dysfunction, 809
Dexamethasone suppression/thyrotropin stimulation test for pituitary pars intermedia dysfunction, 809
Dextran for acute blood loss, 341
Dextran for thromboembolism, 627
Dextrose for neonatal septicemia, 662
Diabetes insipidus, 831
Diabetes mellitus, 829, 831
Diagnostic electrocardiogram, 602
Diaphragmatic hernia, 435
Diarrhea with *Clostridium difficile* infection, 167
Diastolic murmurs
echocardiogram indications for, 614b
in schoolmasters, 573
Diazepam, 19, 460
dosage of, 769t
for foals, 688, 689
for forebrain disease, 769
for inadequate libido, 317
for neonatal sedation, 5
for neonatal seizures, 5
for perinatal asphyxia syndrome, 647, 648t
for pyrrolizidine alkaloid poisoning, 790
DIC. *See* Disseminated intravascular coagulation (DIC)
Dichromatic color vision, 457
Dicosmoecus gilvipes. *See* Caddisfly (*Dicosmoecus gilvipes*)
Dictyocaulis arnfieldi
in foal pneumonia, 666
in interstitial pneumonia, 426
Dicumarol, 354
Didelphis albiventris. *See* White-eared opossum (*Didelphis albiventris*)
Didelphis virginiana. *See* Virginia opossum (*Didelphis virginiana*)
Diencephalon, 764
Diestrus
definition of, 242
endometrial biopsies during, 233
Diet
for colic, 99
for pyrrolizidine alkaloid poisoning, 789
Diet history, 705
Dietary calcium with calcium carbonate calculi, 719
Dietary carbohydrates and cervical stenotic myelopathy, 747
Dietary cation-anion balance (DCAB), 725-726
of equine rations, calculation of, 720b
Dietary copper and cervical stenotic myelopathy, 747
Dietary fat, 815
for exertional rhabdomyolysis, 730-733
Dietary fatty acids for chronic renal failure, 847
Dietary management
of chronic nonsuppurative inflammatory hepatitis, 173
of right dorsal colitis, 142

- Dietary phosphorus, restriction of, 719
Dietary starch and exertional rhabdomyolysis, 730-732
Dietary Supplement Health and Education Act (DSHEA), 26
Dietary supplements for exertional rhabdomyolysis, 730
Dietary thyroid hormone, 815
Dietary zinc and cervical stenotic myelopathy, 747
Differential cell counts
 abnormal, 409-410
 interpretation of, 408-411
Diff-Quik stain, 155, 227, 408, 416
Diffuse microcotyledonary placentation, 245
Diffuse skeletal muscle weakness. *See* Myasthenia
Diflucan. *See* Fluconazole (Diflucan)
Digestibility factor, decrease of, 121
Digestible energy, equations for, 716b, 723b
Digital examination of cervix, 334
Digital flexor apparatus, contracture of, 534-535
Digital flexor tendinitis, extracorporeal shock wave therapy for, 565
Digitalis purpurea, 783
Digits, computed tomography of, 506
Digoxin
 for atrial fibrillation, 607
 for congestive heart failure, 617
 for dysrhythmias, doses of, 604t
 for myocardial disease, 621
 for perinatal asphyxia syndrome, 648t
 for supraventricular tachydysrhythmias, 610
Dilated cardiomyopathy, 620
Dilution kits, 316
Dim light, vision in, 455
Dimethyl sulfoxide (DMSO), 77
 for burns, 224
 for cerebrocortical edema, 770t
 for cervical stenotic myelopathy, 748
 for choledocholithiasis, 172
 for cryopreservation, 282
 for cutaneous habronemiasis, 196
 for EHV-1 myelitis, 754
 for EHV-1 myeloencephalitis, 752
 for EMND, 745
 for endotoxemia, 107
 for forebrain disease, 770
 for interstitial pneumonia, 428
 for jugular vein thrombophlebitis, 626
 for lower motor neuron disease, 752
 for negative-pressure pulmonary edema, 393
 for ocular emergencies, 464t
 for perinatal asphyxia syndrome, 647, 648t
 for peripheral nerve disease, 739
 for peritonitis, 156
 for upper respiratory tract postoperative management, 395
 for viral encephalitis, 770
 in critical care, 20
Dimethyl sulfoxide (DMSO)/thiabendazole/sulfa ointment for equine pastern dermatitis, 202
Dimphylate for mite control, 190
Diocetyl sodium
 for cecal impaction, 140
 for dehydration, 119
Diocetyl sodium—cont'd
 for esophageal obstruction, 93
 for ileal impaction, 130
Diode laser, 394
Dioxin, 90
DIP. *See* Distal interphalangeal joint (DIP)
Diphenhydramine
 for arthropod hypersensitivity, 185
 for atopic dermatitis, 183
 for ergopeptide alkaloid toxicosis, 797
Diptera, 191
Dipyrene
 for endotoxemia, 107
 for foal pneumonia, 672
 for large colon impaction, 133
Direct current conversion for atrial fibrillation, 609
Direct immunofluorescence, 218
Direct immunofluorescence tests, 364
Direct ophthalmic examination, facilitation of, 462
Direct ophthalmoscopy, 450-451
 for vitreous humor examination, 453
Discoid lupus erythematosus (DLE), 177
Disease-modifying osteoarthritis drug (DMOAD), 560
Disinfectants, 25
Disinfection, 25
Disodium cromoglycate for recurrent airway obstruction, 443
Disposable liner for artificial vaginas, 254
Dissecting hematoma of broad ligament, 328
Disseminated intravascular coagulation (DIC), 57, 353-354
 causing intravascular hemolysis, 345
 treatment of, 108
Distal extremities, computed tomography of, 506
Distal hock joints, soreness of, 499
Distal interphalangeal degenerative joint disease (DJD), 498
Distal interphalangeal joint (DIP), collateral ligaments of, 532
Distal intertarsal joints, osteoarthritis, extracorporeal shock wave therapy for, 565
Distal laminae, 532
Distal phalanx
 debridement of, 527
 displacement of, 521
 distal displacement of, 526
 drainage of, 527
 mediolateral rotation of, 526
 osteomyelitis of
 antibiotics for, 526
Distal sesamoidean ligaments, magnetic resonance imaging of, 509
Distal tarsal joints arthrodesis, 540-543
 drilling technique, 540-542
 laser-facilitated, 541-542
Distal tibia, cysts of, computed tomography of, 507
Diuresis with urinary tract calculi, 719
Diuretics for *berteroa incana* toxicosis, 788
Diuretics for congestive heart failure, 621
Diurnal cortisol rhythm with pituitary pars intermedia dysfunction, 809
Diverting loop colostomy, 153f
DJD. *See* Distal interphalangeal degenerative joint disease (DJD)
DMOAD. *See* Disease-modifying osteoarthritis drug (DMOAD)
DMSO. *See* Dimethyl sulfoxide (DMSO)
DNA identification for embryo transfers, 277
DNA-PK. *See* Deoxyribonucleic acid-dependent protein kinase (DNA-PK)
Dobutamine
 for dysrhythmias, 605
 for foals, 691
 for perinatal asphyxia syndrome, 648, 648t
 for shock, 107
Dogbane, 783
Dog-sitting, 70, 321
Domperidone
 and seasonality, 239
 for ergopeptide alkaloid toxicosis, 797-798
 for fescue toxicosis, 323
 for lactation failure, 332
Donkeys, imidocarb diprionate in, 348
Donor mares, selection and management of, 277-278
Dopamine
 for acute renal failure, 843
 for ergopeptide alkaloid toxicosis, 797
 for foals, 691
 for perinatal asphyxia syndrome, 648t
 for shock, 107
Dopamine antagonist and seasonality, 239-240
Doppler echocardiography, 579
 pulmonary outflow velocity, 581f
Dorrance, Tom, 570
Dorsal capsular rotation, 523-524, 523f
Dorsal conchal sinus, 369
Dorsal knot, 326
Dorsal periostitis, extracorporeal shock wave therapy for, 565-566
Dorsal turbinates, examination of, 368
Dorsal ventricular septum, 592
Dorsal-palmar distance, measurement of, 533f
Double inseminations, 268
Double lumen catheters for parenteral nutrition, 114
Double-committed ventricular septal defects (VSD), 596
Double-outlet right ventricle with pulmonary stenosis, 600
Double-outlet ventricle, 594
Doxapram, 652
Doxepin hydrochloride
 for arthropod hypersensitivity, 185
 for atopic dermatitis, 183
Doxycycline, 770
 for Lyme disease, 54
 for ocular emergencies, 463t
DPI. *See* Dry powder inhalant (DPI)
DPJ. *See* Duodenitis-proximal jejunitis (DPJ)
Draft horses
 atrial fibrillation
 ambulatory electrocardiogram, 609f
 atropine for, 557
 equine polysaccharide storage myopathy in, 728
 squamous cell carcinoma in, 480
Draschia, 767
Draschia megastoma, 195, 775
Draught horses, exercise-induced pulmonary hemorrhage in, 429
Dressage horses, 384
 distal hock joints soreness in, 499
 prepurchase examination of, 493
 with exercise intolerance, 416

- Dressings for thermal burns, 222
 Dromosedan. *See* Detomidine hydrochloride (Dromosedan)
 Dropped elbow, Hackney pony with, 736
 Drug absorption, 7-9
 Drug delivery devices
 aerosolized, 436-440
 disadvantages of, 437
 Drug dosage, optimization of, 9
 Drug testing
 in performance horses, 32-35
 methodology of, 32-34
 samples of, 32
 split sample analysis, 34
 in preperformance purchase, 499
 Drug toxicity, hematuria, 854
 Drug-induced nephrotoxicity, risk factors for, 840b
 Dry needling, 569
 Dry powder inhalant (DPI) devices, 439-440
 DSHEA. *See* Dietary Supplement Health and Education Act (DSHEA)
 D-transposition of the great vessels, 600
 Dual-tipped high-fidelity Millar catheter, pressure tracings of, 590f
 Duct tape for foot, 547
 Ductus arteriosus, 592
 persistent patency of, 592
 Dulbecco's phosphate buffered saline for embryo collection, 280
 Duodenal stenosis, weanling with, 102f
 Duodenal ulcer in foals, 96
 Duodenitis-proximal jejunitis (DPJ), 120-123
 clinical pathology of, 122
 clinical signs of, 121-122
 diagnosis of, 122
 mechanisms of, 121f
 pathology of, 120
 pathophysiology of, 121
 prognosis of, 123
 treatment of, 122-123
 Duodenoscopy of foals, 685
 Duodenum, examination of, 148
 Duragesic in critical care, 20
 Dust particles affecting heaves, 420
 Dye excretion tests, 170
 Dynamic lesion, 747
 Dysgerminomas of ovaries, 262
 Dysphagia, 773
 Dyspnea, 401
 Dysrhythmias, 602-613
 electrocardiography of, 602-603
 left ventricle, 587f
 medications for
 doses of, 604t
 Dystocia, 245, 327
 causing retained fetal membranes, 330
 cervical lacerations associated with, 334
 effect on peritoneal fluid, 296
 etiology of, 320
 incidence of, 319
 management of, 320-321
 Dystrophic epidermolysis bullosa, 219
- E**
 Ear infestations with ticks, 189
 Ear nets, 191
 Early breeding, 237
 Early embryonic vesicle confusion with endometrial cyst, 246
 Early postoperative management of the orthopedic patient, 544
 Easley, Jack, 86
 Eastern equine encephalitis (EEE), 194, 766, 774
 Easy-keepers, 814
 EAV. *See* Equine arteritis virus (EAV)
 Echium, 789
 Echocardiography, 577-584
 after exercise, 589
 in myocardial disease, 621
 for acquired pericardial disease, 622-623, 623
 for aortic aneurysms, 624
 for aortic regurgitation, 618
 for mitral regurgitation, 615-616
 for myocardial disease, 620
 for ventricular ectopy, 611
 scanning technique for, 580-584
 Echogenic fibrous bands, 261
 Echthiophate (phospholine iodide) for skin parasites, 196
 Eclipse refractometer, 323
 Ectoparasites, 188t
 Ectopic beats, 610-611
 Ectopic lacrimal punctum, 490
 Ectopic ureter, 826-827
 EDDI Equine. *See* Ethylene diamine dihydroiodide (EDDI Equine)
 Edema, 846
 of endometrium, 244
 treatment of, 303
 Edetic acid, 437
 EDM. *See* Equine degenerative myeloencephalopathy (EDM)
 EDTA. *See* Ethylenediaminetetraacetic acid (EDTA)
 EEE. *See* Eastern equine encephalitis (EEE)
 EGAD. *See* Equine grain associated diseases (EGAD)
 EGE. *See* Equine granulocytic ehrlichiosis (EGE)
 Egg bar shoes, 525, 536
 Egg reappearance time (ERT), 162
 EGUS. *See* Equine gastric ulcer syndrome (EGUS)
 EHM. *See* Equine herpesvirus myeloencephalopathy (EHM)
Ehrlichia phagocytophilia, 78
Ehrlichia risticii, 74
 EHV. *See* Equine herpesvirus (EHV)
 EHV-1. *See* Equine abortion virus (EHV-1)
 EHV-2. *See* Equine cytomegalovirus (EHV-2)
 EHV-4. *See* Equine rhinopneumonitis (EHV-4)
 EHV-1 myeloencephalitis
 flunixin meglumine for, 752
 keratitis secondary to, 475
 ocular signs secondary to, 476
 prognosis of, 754-755
 EIA. *See* Equine infectious anemia (EIA)
 EIAD. *See* Extended-interval aminoglycoside dosing (EIAD)
 EIAV. *See* Equine infectious anemia virus (EIAV)
Eichium, 768
 EIPH. *See* Exercise-induced pulmonary hemorrhage (EIPH)
 Eisenmenger's physiology, 598
 EIV. *See* Equine influenza virus (EIV)
 Ejaculated semen
 blood in, 306
 cryopreservation of
 preparation of, 270
 environmental influence on, 266-267
 freezing procedure for, 270-271
 motility assessment of, 267
 Ejaculated semen—cont'd
 screening for poor quality, 267
 thawing procedure for, 271
 total spermatozoal number in calculation of, 267
 Ejaculates with low sperm count, 256
 Ejaculation, dysfunction of, 318
 Ejection fraction, 580
 Ejection murmurs, 595, 598
 ELA. *See* Equine leukocyte antigens (ELA)
 Elastosis, 235
 Elbow joint flexion, reduction of, 735
 Elbow lock, 320
 Electrical burns, management, 224
 Electrified insect light trap, 191
 Electroacupuncture, 569
 Electrocardiogram, 576
 analysis of, 577
 definition of, 576
 during exercise, 586-587
 in acquired pericardial disease, 622
 in myocardial disease, 620
 in ventricular ectopy, 610-611
 interpretation of, 602
 measurements in, 577
 ventricular premature depolarization in standing horse, 588f
 Electrodiagnostics in cranial nerve diseases, 777
 Electrohydraulic lithotripsy for cystic calculi, 833
 Electrohydraulic shock wave generator, 563f
 Electrolytes
 abnormalities of in peritonitis, 154
 alteration of, 846
 for anhidrosis, 817
 for brainstem disease, 777
 for dehydration, 119
 for exertional rhabdomyolysis, 730
 for foal diarrhea, 678
 for negative-pressure pulmonary edema, 393
 fractional clearance of, 821, 822t
 in parenteral nutrition, 113
 Electromagnetic generator, 563f
 Electromyography (EMG) for peripheral nerve disease, 739
 Electronic peristaltic pumps, 459
 Elephant on a tub stance, 741
Elimia livescens. *See* Snail (*Elimia livescens*)
 ELISA. *See* Enzyme-linked immunosorbent assay (ELISA)
 Elspar. *See* L-asparaginase (Elspar)
 Embolization microcoils, 390
 Embryonic vesicles
 manual reduction of, 246
 natural reduction of, 246
 ultrasound image of, 232f
 Embryos
 collection of, 280-281
 cooling of, 280-281
 loaded into semen straw, 283f
 storage of, 281-282
 transfer of, 277, 283-285
 permits for, 277
 EmCare Complete Flush Solution, 280, 286
 EME. *See* Equine monocytic ehrlichiosis (EME)
 Emergency kit for postpartum hemorrhage, 327-328, 328t
 Emergency ocular examination, 462
Emerella nidulans, 389
 EMG. *See* Electromyography (EMG)

- Emollient for vaginal lacerations, 327
- Enalapril
for aortic regurgitation, 618
for dysrhythmias, 604t
for ventricular ectopic beats, 611
- Encephalitis, 800
- Endocardial cushion, 592, 592f
defect of
in foal, 592f
- Endocrine maturation, 641
- Endogenous erythropoietin, 343
- Endogenous mediators, prevention of
synthesis, release or action of, 107
- Endometrial biopsy, 233-234
- Endometrial cells, examination of, 227-228
- Endometrial culture, 229-231
interpretation of, 230
sampling technique for, 229
- Endometrial cysts, 231
confusion with early embryonic vesicle, 246
ultrasound image of, 232f
- Endometrial cytology, 226-228
- Endometrial swabs, 229
- Endometriosis, susceptibility to, 234
- Endometritis
and embryo transfers, 277
etiology of, 272
- Endometrium
edema of, 244, 272
of foaling mare
cytologic evaluation of, 272
- Endophthalmitis, 466
- Endophyte, exposure of causing retained
fetal membranes, 330
- Endoscopic microbiology aspiration
catheter, 402
- Endoscopy
for arytenoid chondrosis, 381
for cranial nerve diseases, 777
for exercise-induced pulmonary
hemorrhage in thoroughbred
horses, 430
for guttural pouch empyema, 387
for guttural pouch mycosis, 389
for progressive ethmoid hematoma,
375-376
of exercising horse, 368-369
of nasal passages, 370, 372-373
of sport horses with exercise
intolerance, 416
of urinary tract, 822
portals for, 372
- Endosperm, 106
- Endothelial cell dysfunction, insulin
insensitivity, 813
- Endotoxemia, 57, 104-108, 469, 831
and retained fetal membranes, 331
cause of, 124
clinical signs of, 105
diagnosis of, 105
in pregnant mares, 108
management of, 105-108
pathophysiology of, 104-105
- Endotoxin
causing disseminated intravascular
coagulation, 353
components of, 104
drug therapy of, 21
neutralization of, 106-107
prevention of release into circulation,
105-106
- Endotoxin-induced cellular activation
prevention of, 107
- Endotoxin-induced coagulopathy, 108
- End-tidal carbon dioxide monitor in
cardiopulmonary resuscitation of
foals, 654
- Endurance horses, exercise-induced
pulmonary hemorrhage in, 429
- Energy
determining requirements for, 112
feeding for, 698-701
in parenteral nutrition, 112
requirements of, 698, 715
in acutely ill horse, 707
source of influence on health, 701-702
- Energy concentrates, 701
- Energy fluence, 394
- Energy sources, 698-699
and performance, 702-703
- Enilconazole (Imaverol)
for equine pastern dermatitis, 203
for folliculitis, 200
for guttural pouch mycosis, 389
- Enlarged ovaries, 261-263
- Enophthalmos, 462
- Enrofloxacin for pleuropneumonia, 424
- Enteral feeding
for large colon impaction, 134
for neonatal septicemia, 662
for perinatal asphyxia syndrome, 649
importance of, 114-115
of acutely ill horse, 708-710
- Enteritis in septic foals, 657
- Enterobacter*, 6, 10, 838
- Enterococci in foals, 3
- Enterolithiasis, 99, 149, 725-726
- Enterotomy, 723
- Entrolyte He, 817
- Environmental control
of interstitial pneumonia, 428
of uveitis, 470
- Environmental factors
affecting spermatozoa, 266
and cervical stenotic myelopathy, 747
in heaves, 420
- Environmental temperature during
thermography, 503-504
- Enzyme-linked immunosorbent assay
(ELISA), 46, 52
- ergopeptide alkaloid concentrations,
797
- for allergy testing, 182
- for *Clostridium difficile* infection, 167
- for equine infectious anemia, 347
- for equine monocytic Ehrlichiosis, 76
- for foal pneumonia, 679
- for neonatal septicemia, 658
- for *Rhodococcus equi* infections, 61
- for von Willebrand's disease, 352
- in drug testing, 33
- of tapeworm diagnosis, 159
- Eosinophilic enterocolitis, 147
clinical signs of, 145t
idiopathic, 147
- Eosinophilic gastroenteritis, 147
- Eosinophilic keratoconjunctivitis, 478
- Eosinophilic pericarditis, 622
- Eosinophils, 228
in bronchoalveolar lavage, 409
in tracheal aspirates, 405
- Epicauda atrivittata*, 785
- Epicauda* (blister beetle), 89
- Epicauda funebris*, 784
- Epichloe typhina*, 796
- Epidermolysis bullosa, 219
- Epidermolysis bullosa simplex, 219
- Epidural anesthesia
for dystocia, 320
for rectal tears, 152
- Epidural neoplasms, 775
- Epiglottis
examination of, 366-367
stiffness of, 367
- Epilepsy, 771
- Epinephrine
for cardiopulmonary resuscitation of
newborn foal, 653
for urticaria, 206
- Epiphora, 478
vs. excessive lacrimation, 489-490
- Epiploic foramen, entrapments within,
125
- Epistaxis, 340, 375, 388
incidence of, 430
with exercise-induced pulmonary
hemorrhage, 429-430
- Epithelial cells in tracheal aspirates, 404
- Epitheliogenesis imperfecta, 219
- Epitheliotropic lymphosarcoma, 209
- EPM. *See* Equine protozoal
myeloencephalitis (EPM)
- Epogen. *See* Recombinant human
erythropoietin (Epogen)
- Epsilon-aminocaproic acid (Amicar) for
acute blood loss, 341
- EPSM. *See* Equine polysaccharide storage
myopathy (EPSM)
- EqStim, 446
- Equimmune IV, 447
- Equine abortion virus (EHV-1), 474t
causing interstitial pneumonia, 426
- Equine adenovirus, 88, 474
- Equine AeroMask, 437, 438f, 439
- Equine Aerosol Delivery Device System,
438, 438f
- Equine arteritis virus (EAV), 52
spread from stallions to mares, 252-253
- Equine Clinical Nutrition*, 706
- Equine coital exanthema, 41, 305-306
- Equine coital exanthema virus (EHV-3),
474t
- Equine Cushing's disease, 807-811
- Equine cytomegalovirus (EHV-2), 474t
keratitis secondary to, 475
- Equine degenerative
myeloencephalopathy (EDM),
748-749
- Equine Digital Support System, 523
for digital flexor apparatus contracture,
534
- Equine ehrlichiosis, 348
- Equine encephalomalacia associated with
signs of forebrain disease, 765-766
- Equine eosinophilic granuloma, 206-207
- Equine fescue toxicosis, 796
- Equine gastric ulcer syndrome (EGUS),
94-98
clinical syndromes, 95-96
diagnosis of, 96
pathogenesis of, 94-95
treatment of, 96-98, 97t
- Equine glaucoma, 486-488
- Equine grain associated diseases (EGAD),
701
- Equine granulocytic ehrlichiosis (EGE),
78-80
clinical signs of, 78-79
diagnosis of, 79-80
epidemiology of, 78
etiology of, 78
immunity to, 79

- Equine granulocytic ehrlichiosis (EGE)—
cont'd
pathology of, 79
prevention of, 80
treatment of, 80
- Equine grass sickness differentiation of, 743t
- Equine Haler device, 438f, 439
- Equine herpesvirus (EHV), 52, 88, 469
abortion, 40-41
clinical syndromes associated with, 474t
differential diagnosis of, 474-475
ocular manifestations of, 473-476
with penile paralysis, 304
- Equine herpesvirus-1 (EHV-1), 750, 766
- Equine herpesvirus keratitis, 451
- Equine herpesvirus
myeloencephalopathy (EHM), 39-40, 756
- Equine hyperelastosis cutis, 219
- Equine infectious anemia (EIA), 45-47, 88, 346-347
clinical signs of, 45-46
control of, 46-47
diagnosis of, 46
transmission of, 46
with penile paralysis, 304
- Equine infectious anemia virus (EIAV), 45-47
- Equine influenza virus (EIV), 42-44, 474
clinical signs of, 42-43
diagnosis of, 43
management of, 42-43
prevention of, 43
- Equine leukocyte antigens (ELA), 204
- Equine metabolic syndrome, 701, 812-815
- Equine metritis, 229-230
- Equine monocytic ehrlichiosis (EME), 74-77
biology of, 74-75
clinical pathology of, 76
clinical signs of, 75-76
diagnosis of, 76
epidemiology of, 74-75
life cycle of, 74-75
necropsy findings of, 76-77
prevention of, 77
treatment of, 77
- Equine motor neuron disease, 739
confirmation of, 744
- Equine pastern dermatitis, 201-203
clinical signs of, 201
diagnosis of, 201-202
pathogenesis of, 201, 202b
treatment of, 202-203
- Equine polysaccharide storage myopathy (EPSM), 728
- Equine protozoal myelitis, 754, 756, 766
- Equine protozoal myeloencephalitis (EPM), 29, 69-74, 749, 773-774
clinical signs of, 69-71
diagnosis of, 71-72
diagnostic rule-outs, 71
epidemiology of, 69
life cycle, 69
prevention of, 73-74
treatment of, 72-73
relapse, 73
- Equine protozoal myeloencephalopathy, 735
- Equine recurrent uveitis (ERU), 468-473, 478
classic, 468-469
clinical signs of, 468
- Equine recurrent uveitis (ERU)—cont'd
diagnosis of, 469
histologic features of, 469
incidence of, 470, 470t
insidious, 468-469
organisms associated with, 468-469
prevalence of, 468
surgical techniques for, 472t
therapy of, 470-473
treatment of, 469-473
- Equine rhinopneumonitis (EHV-4), 474t
- Equine sarcoid, 203-205
cryotherapy of, 204-205
diagnosis of, 204
hyperthermia of, 205
immunotherapy of, 205
laser ablation of, 204
radiotherapy of, 205
sites of, 204
surgical excision of, 204
treatment of, 204-205
- Equine Senior, 723
- Equine sleeping sickness, 766
- Equine viral arteritis, 469
- Equine viral arteritis (EVA), 36-38, 363-364, 474
carrier state of, 36-37
causing interstitial pneumonia, 426
clinical signs of, 36-37
diagnosis of, 37
oral ulceration with, 88
pathogenesis of, 37
pathology of, 37
prevention of, 37-38
testing for
prior to semen collection, 269
treatment of, 37-38
with penile paralysis, 304
- Equi-Pak, 525
- Equiproxen. *See* Naproxen (Equiproxen)
- Equitainer, 268, 281
- Equi-Thane, 525
- EQUI-Z, 694
- Equus caballus*, chromosomes in, 261
- Erection dysfunction, 318
- Ergocornine, 796
- Ergocristine, 796
- Ergocryptine, 796
- Ergogenic nutraceuticals, 28-29
- Ergonovine, 796
- Ergonovine maleate in critical care, 21
- Ergopeptide alkaloids, 779, 796
toxicoes, 796-798
- Ergosine, 796
- Ergot alkaloid binders, therapeutic
efficacy of, 797
- Ergot alkaloids, 796
toxicosis, 796-797
- Ergotamine, 796
- Ergotism, 796
- Ergovaline, 796
- ERT. *See* Egg reappearance time (ERT)
- ERU. *See* Equine recurrent uveitis (ERU)
- Erythema multiforme, 177
cutaneous lesions of, 89
histopathology of, 178
- Erythrocyte antigens, 355
- Erythrocytosis, 358
- Erythromycin, 10, 770
dosage optimization of, 9
for cecal impaction, 140
for equine monocytic Ehrlichiosis, 77
for foal pneumonia, 671, 673
for ileus, 110-111
- Erythromycin—cont'd
for perinatal asphyxia syndrome, 648, 648t
for proliferative enteropathy, 165
for *Rhodococcus equi* infections, 62
interfering with thermoregulation, 676
neonatal absorption of, 1
neonatal metabolism of, 3
oral administration of, 7
- Erythropoietin, 342
- Escherichia coli*, 6, 11, 38
complicating burns, 224
in foal pneumonia, 666-667
in foals, 3
in jugular vein thrombophlebitis, 626
in neonatal septicemia, 660
in placental hydrops, 302
in placentitis, 297
in retained fetal membranes, 330
in semen, 255
- Esophageal balloon catheter, 415
- Esophageal endoscopy for esophageal obstruction, 91
- Esophageal obstruction (choke), 90-94
anatomy of, 90-91
clinical signs of, 91
diagnosis of, 91-93
prevention of, 94
treatment of, 93-94
- Esophageal radiography for esophageal obstruction, 91-92
- Esophageal ultrasound for esophageal obstruction, 92-93
- Esophagus, anatomy of, 90-91
- Essential fatty acids
for atopic dermatitis, 182-183
in parenteral nutrition, 112-113
- Estradiol
causing estrus onset delay, 249-250
for incontinence, 825
for recipient mares, 279
in subfertile stallions, diagnostic
measurement of, 258
production of, 261
- Estrogen, 257
demonstrating placentitis, 300
for upward fixation of the patella, 537
- Estrus
definition of, 242
detection of, 264
endometrial culture during, 229
failure to show, 264
onset delay of, 249-250
pharmacologic induction of, 239-240
staging of, 242-245
- Estrus cycle
early induction of, 237
length of, 242
related performance problems, 265
- Ethmoid hematoma, 340
diagnosis of, 373, 374
- Ethmoid turbinates
examination of, 368
normal appearance of, 368fz
- Ethyl lactate for equine pastern dermatitis, 202
- Ethylene diamine dihydroiodide (EDDI Equine) for sporotrichosis, 214
- Ethylene glycol for cryopreservation, 282
- Ethylenediaminetetraacetic acid (EDTA), 350, 437
for corneal lacerations, 465
for ocular emergencies, 463t
- Etodolac for colic, 117

- Eupatorium adenophorum*. See Crofton weed (*Eupatorium adenophorum*)
- Eupatorium rugosum*, 783, 783f
- European warmbloods, 498
- Euthanasia
for intestinal rupture, 155
for plasma cell myeloma, 362
for rectal tears, 152
- Eutocia, 326
- EVA. See Equine viral arteritis (EVA)
- Eventers, prepurchase examination of, 493
- Excessive residual mucosa complicating arytenoidectomy, 383
- Exercise
and arrhythmia, electrocardiography of, 578f
and cervical stenotic myelopathy, 747
and chronic exertional rhabdomyolysis
feeding recommendations for, 731t
echocardiography after, 589
electrocardiography during, 586-587
for breeding stallions, 252
for hydroceles, 307
for penile trauma, 303
Exercise electrocardiography for aortic regurgitation, 618
Exercise intolerance, 401, 589
bronchoalveolar lavage, 411
in dressage horses, 416
sport horses with, 416-417
with laryngeal hemiplegia, 384-385
Exercise stress echocardiography, 589
Exercise studies, 413
Exercise-associated hematuria, 856
Exercise-induced pulmonary hemorrhage (EIPH), 340, 401, 429-433
and airway inflammation, 430
and upper airway resistance, 432-433
bronchoalveolar lavage, 410-411
chest radiography of, 431
diagnosis of, 431
effects of, 431
etiology of, 430
resembling progressive ethmoid hematoma, 375
treatment of, 431-432
Exercising horse
axial deviation of the aryepiglottic folds in, 379f
endoscopy of, 368-369
Exertional rhabdomyolysis
chronic, 727-728
feeding recommendations for, 731t
clinical signs of, 727
diagnosis of, 728-729
dietary fat supplementation for, 732-733
differential diagnosis of, 727
etiology of, 727-728
fat supplementation for, 733
nutritional management of, 727-728, 727-734
pathophysiology of, 727-728
Exfoliative dermatitis, 177
histopathology of, 179
Exfoliative eosinophilic dermatitis, 89
Exhalation flow rates, 437
Exogenous photodynamic agents, 175t
Exogenous thyroid hormone
supplementation, annual cost of, 251
Exogenous vasopressin administration, 822
Exophthalmos in sinus disease, 369
Expected foaling date, calculation of, 323
Expectorants
for foal pneumonia, 672
for heaves, 420
Exploratory celiotomy
for intestinal rupture, 155
ileal impaction during, 130f
Exposure keratitis, 465, 476
secondary to neurologic disease, 476
treatment of, 476
Extended trot
in prepurchase examination, 497
navicular disease affecting, 498
Extended-interval aminoglycoside dosing (EIAD), 850
External cervical os, 334
External genitalia, squamous cell carcinoma of, 836
Extracorporeal shock wave therapy, 562-566
analgesic effect of, 565
biologic effects of, 565
complications of, 566
equine applications of, 565-566
Extramural obstruction, 490
Extravascular hemolysis, 345-346
Eye
examination of, 450-454, 451-452
extranodal lymphoma of, 360
neuroophthalmic examination of, 451-452
Eye pain of unknown explanation, 462
Eyelids
asymmetry of, 462
blocking ocular infection, 477
damage of, 224
drooping of, 462
lacerations of, 464-465
surgical repair of, 465
margins of, perfect apposition of, 465
Eyes, molds in, 792
F
Face
asymmetry of, 462
swelling of in sinus disease, 369
Face flies, 194
Facemask, 415, 439
Facet arthritis, computed tomography of, 507
Facial paralysis in cranial nerve diseases, 772
Facilities design for infection control, 25
Factor VIII deficiency, 351
Facultative anaerobic bacterial pathogens with foal diarrhea, 679
Failure of passive transfer (FPT), 649, 656
in foals, 693
False lupin, 782
False-positive reactions to intradermal allergy test for atopy, 182
Fat, 698
public health effects of, 701
saturation images of, 509
sources of, 731
substituted for starch and sugar, indications for, 702b
supplementation of for exertional rhabdomyolysis, 733
suppression images of, 509
Fatigue, 702
Fat-soluble vitamins for chronic nonsuppurative inflammatory hepatitis management, 173
Fatty acids
as energy source, 112
for arthropod hypersensitivity, 185
FDE. See Fixed drug eruptions (FDE)
FDP. See Fibrin degradation products (FDP)
Fecal cytotoxin assay, 167
Fecal enema for *Clostridium difficile* infection, 168
Fecal flotation detection of tapeworm eggs, 158-159
Fecal gram staining for *Clostridium difficile* infection, 168
Fecal worm egg counts (FWEC), 161
McMaster technique for, 162
Feed
assessment of, 705-706
bulk pelleted, 723
containing probiotics, 712-713
deprivation of, 95
dietary cation-anion balance
calculation of, 720b
digestible energy values, 700t
energy content of, 698
formulation of, 704
mineral content of, 721t
restriction of for resistant cyathostomiasis, 164
sweet, 810
toxicoses, 779
Feed additives, 27
Feed bumps, 206
Feeding
for breeding stallions, 252
for colic, 99
for energy, 698-701
recommendations for, 703-704
Feeding protocol, 706
Feeding volume, 717
Feet
bandaging of, 547
cast for, 549-550
application of, 550f
evaluation of for breeding stallions, 252
lameness of
in performance horse, 500
temperature of, 503
mange of, 187
proton density image of, 512f
rigid immobilization of in cast
application, 549
structural changes to, 528-529
Feline immunodeficiency virus (FIV), 45
Fell ponies, peripheral ganglionopathy of, 696-697
Female fetus
at 90 days, ultrasound of, 290f
at more than 100 days, ultrasound of, 289f
Female gonads, distinguishing features of, 293f
Fenbendazole
cyathostomiasis resistance to, 162
for brainstem disease, 777
Fenestration, 541
Fenoterol, 437
for heaves, 419
Fentanyl, 20
Fenthion, 196
Fermentable carbohydrates, 698
Ferrous sulfate for chronic blood loss, 341
Fertility
anabolic steroid effect on, 261
and endometrial cysts, 232

- Fertility—cont'd
 and thyroid function, 250-251
 cryopreserved semen vs. cooled semen, 274
 hemospermia effect on, 306
 hydrocele effect on, 306
 of stallion, prediction of, 272
- Fescue
 acremonium-infected, 633
 causing retained fetal membranes, 330
 toxicosis, domperidone for, 323
- Festuca arundinacea*, 796
- Fetal compromise
 prepartum maternal signs of, 631-632
 prognosis of, 634-635
- Fetal cortisol, 641
- Fetal diarrhea, 633
- Fetal gender
 determination of, 288-294
 materials for, 288
 procedure for, 288-289
 ultrasound, 289f
- Fetal malpositioning causing angular limb deformities, 663
- Fetal meconium aspiration, 645
- Fetal membranes
 evaluation of, 324
 retention of, 245
- Fetal triiodothyronine (T3), 641
- Fetlock joint
 computed tomography of, 506
 hold of, 545f
 of racehorse, 501
 radiography of, 498
 temperature of, 503
- Fetotome, 320, 321
- Fetuses
 aorta, diameter of, 632
 caudal presentation of, 320
 deformity of, transverse presentation with, 321
 dorsopubic position of, 321
 heart rate of, 632
 in caudal abdomen, ultrasound of, 247f
 infection of causing dystocia, 320
 tibia-tailhead triangle, 293
 transverse presentation of, 320
 twin. signs of, 632
 ultrasound of
 at 60 days, 289f, 290f
 at 90 days, 290f
 at more than 100 days, 289f
- Fever, 401
- FFA. *See* Free fatty acids (FFA)
- Fiber substituted for starch and sugar, indications for, 702b
- Fiberglass cast, 549
- Fiberoptic bronchoscopy, 407
- Fiberoptic endoscopy for tracheal aspiration, 402
- Fibrin, 623
 in neoplastic effusions, 424
 in pleuropneumonia, 421
- Fibrin degradation products (FDP), 350
 for heaves, 420
- Fibroblastic sarcoids, 203
- Fick principle, 591
- Field of view, 455
- Filters for artificial vaginas, 254
- Filtration gonioimplants for glaucoma, 487-488
- Fine needle aspiration, 482
- Finoff transilluminator, 450, 451
- Fipronil. *See* Phenylpyrazole (fipronil)
- Fipronil for equine pastern dermatitis, 203
- First heart sound (S1), 575
- First phalanx, cystic lesions of, computed tomography of, 506
- First-degree atrioventricular block, 603-604
- First-degree burns, 220
- Fistulation of auditory tube diverticulum, 388
- FIV. *See* Feline immunodeficiency virus (FIV)
- Fixed drug eruptions (FDE), 178
- Flaccid paraphimosis, 304
- Flail thorax, 435-436
- FLAIR strips for exercise-induced pulmonary hemorrhage, 432
- Flame spectrophotometer, mammary secretion electrolytes, 315
- Flatweed, 739
- Flavivirus encephalitides, 49-50
- Flavivirus encephalitis, 766
- Flecainide for atrial fibrillation, 609
- Flexible endoscope vs. arthroscopy, 372
- Flexible fiberoptic endoscopes, 366
- Flexion tests, 497
- Flexor tendons
 magnetic resonance imaging of, 509
 palpation of, 496
- Flexural deformities causing dystocia, 320
- Flies
 control of, 185, 191-195, 192b, 196
 life cycle of, 191
- Floctymetric analysis of sperm membranes, 272
- Flowmetrics, 415
- Fluconazole (Diflucan), 479t
 for ocular emergencies, 463t
- Fluid bronchogram of pulmonary consolidation, 422f
- Fluid, calculation of, worksheet for, 118t
- Fluid pressure of stifle, 496
- Fluid therapy
 for brainstem disease, 777
 for colic in foals, 685-686
 for ileal impaction, 128
 for neonatal septicemia, 660
 for perinatal asphyxia syndrome, 647-648
- Flumethrin for equine pastern dermatitis, 203
- Flunixin meglumine (Banamine)
 for cantharidin toxicosis, 785, 786
 for cecal impaction, 140
 for colic, 116
 for colic in foals, 686
 for disseminated intravascular coagulation, 353
 for duodenitis-proximal jejunitis, 123
 for EHV-1 myelitis, 754
 for EHV-1 myeloencephalitis, 752
 for endotoxemia, 107
 for endotoxemic mares, 108
 for endotoxin, 21
 for equine protozoal myelitis, 754
 for equine recurrent uveitis, 471t
 for fetal compromise, 632
 for foal pneumonia, 672
 for foals, 691
 for glaucoma, 487
 for interstitial pneumonia, 428
 for joint disease, 559
 for jugular vein thrombophlebitis, 626
 for large colon impaction, 133
- Flunixin meglumine (Banamine)—cont'd
 for negative-pressure pulmonary edema, 393
 for neonates, 4, 5
 for ocular emergencies, 463t, 464, 464t
 for peritonitis, 156
 for permanent tracheostomy in standing horses, 397
 for placental hydrops, 302
 for placentitis, 300
 for pleuropneumonia, 424
 for postpartum hemorrhage, 330
 for rectal tears, 152
 for retained fetal membranes, 332
 for small intestine strangulating obstruction, 124, 126
 for strangles, 66, 67
 for thermal burns, 222
 for transvaginal reduction, 247
 for uveitis, 468
 in critical care, 20
 toxicity of, 559
- Fluorescein sodium, 451
 for corneal ulcers, 478
- Fluorescein sodium dye
 for conjunctival chemosis, 465
 for nasolacrimal drainage evaluation, 465
 inhibiting herpesviruses, 475
 to evaluate corneal epithelial integrity, 462
- Fluorescein uptake of intestinal viability, 137
- Fluorescence polarization, 46
- Fluorescent antibody testing for sporotrichosis, 214
- Fluoroquinolone, 6
 dosage optimization of, 9
 for choledocholithiasis, 172
 for foal diarrhea, 679
- 5-fluorouracil (5-FU)
 for equine sarcoid, 205
 for penile squamous cell carcinoma, 305
 for squamous cell carcinoma, 836
- Fluphenazine for ergopeptide alkaloid toxicosis, 798
- Flurbiprofen
 for equine recurrent uveitis, 471t
 for glaucoma, 487
 for ocular emergencies, 464t
- Flush medium for embryo collection, 280
- Fluticasone propionate
 for heaves, 419
 for recurrent airway obstruction, 442, 444
- Fly masks, 194
- Foal diarrhea, 677-680, 713
 nutritional causes of, 677
- Foal heat diarrhea, 677
- Foal heat-breeding, 248-250
 and ovulation time, 249
 clinical examination for, 249
- Foal limb malpositioning, 333
- Foal pneumonia, 666-674
 clearing secretions in, 672
 clinical presentation of, 668-669
 diagnosis of, 669-671
 epidemiology of, 667
 etiology of, 666-667
 maintaining gas exchange in, 672-673
 pathogenesis of, 667-668
 prevention of, 673-674
 treatment of, 671-673
- Foal Resuscitator, 651

- Foaling
 effect on peritoneal fluid, 296
 history, 322-323
- Foaling mare
 endometrium of, cytologic evaluation of, 272
 examination of, 249
- Foaling stall, 323
- Foals. *See also* Neonatal
 anesthesia for, fatality rates in, 689t
 cardiovascular parameters
 interdependence, 687b
 colic in, 680-686
 congestive heart failure in, 596
 corrective shoeing of, 531
 cranial presentation of, 320
 duodenoscopy of, 685
 endocardial cushion defect in, 592f
 gastric outflow obstruction in, 101-103
 gastric ulceration in, 95-96
 gastrosocopy of, 685
 general anesthesia of, 687-691
 hand-feeding of in isolation, 265
 immunodeficiencies of, 692-699
 iron deficiency in, 343
 iron metabolism in, 343
 mare ambivalence towards, 264
 mare avoidance of, 265
 mare extreme protectiveness toward, 264
 mare savage attacks on, 265
 mare stealing of, 265
 mares fearing, 265
 nasal insufflation of, 428
 neonatal, 633-634
 normal blood volume of, 640
 nutritional assessment of, 661
 perinatal asphyxia syndrome, 644-649
 perioperative fatality rate in, 687t
 peritoneal fluid analysis in, 684-685
 physiology of, 687-688
 resuscitation of, 653f
 salmonellosis in, 679
 sedation of, 688-691
 sheared heels in, 529
 thoracic compressions in, 652
 tricuspid regurgitation in, 575
 tube-feeding of, 265
 viability after birth, 315
 with proliferative enteropathy, 165
 with ruptured bladders, 681
- Foam cast padding, 549
- Focal encephalitis-mylitis, 69
- Focal light source, 450, 453
 for corneal defects, 475
 for emergency ocular examination, 462
 for vitreous humor examination, 453
- Focal retinal detachments, 467
- Fog fever, 675
- Foley catheter, 326
- Folic acid
 for chronic nonsuppurative
 inflammatory hepatitis
 management, 173
 in parenteral nutrition, 113
- Follicle stimulating hormone (FSH), 257
 for artificial insemination preparation, 272
 in subfertile stallions, diagnostic
 measurement of, 258
- Follicle, ultrasound image of, 243-244, 243f
- Follicular development, monitoring of, 245
- Follicular phase, estrus cycle, length of, 242
- Folliculitis, 197-200
- Fomites, 24
- Food and Drug Administration Center for
 Veterinary Medicine on
 compounding drugs, 31
- Food deprivation, effects on stressed
 catabolic animals, 112
- Forages, 698-700
 potassium content of, 721
- Foramen ovale, 592f, 646
 membrane of
 two-dimension echocardiogram of, 592f
- Forced expiratory maneuvers, 415
- Forced oscillatory mechanics, 415
- Forebrain, 764
- Forebrain disease
 cerebrospinal fluid analysis, 768-769
 clinical signs of, 764-765, 768
 diagnosis of, 767-769
 diseases manifesting with signs of, 765-766, 765b
 hematology of, 768
 history, 767-768
 metabolic causes of, 767
 prognosis of, 769-770
 serology, 769
 serum chemistry of, 768
 signalment, 767-768
 treatment of, 769-770
- Foreign objects, 465, 474
- Forelimb, examination of, 496
- Formaldehyde for acute blood loss, 341
- Formaldehyde gas, 377
- Formalin, 364, 377
 in critical care, 21
- Formoterol for recurrent airway
 obstruction, 444
- Formulas for parenteral nutrition, 114t
- Fossa cysts, 261
- Fossa glandis, aerobic bacterial cultures
 of, 269
- Four-point rail shoe, 523f
- Four-point shoe, application of with
 laminitis, 524f
- Fourth heart sound (S₄), 575
- Foxglove, 783
- FPT. *See* Failure of passive transfer (FPT)
- Fractional shortening, 580
 decreased, 589
- Fractured ribs, 435-436
 location of, 436
- Fractures
 cysts of, computed tomography of, 507
 shock wave therapy for, 565
- Free fatty acids (FFA), increased
 mobilization of, 702
- Free thyroid hormone, 250-251
- Free-floating echogenic spots, 261
- Free-hand injection technique, 247
- Freezing procedure for ejaculated semen,
 270-271
- French guiding catheter, inner catheter
 within, 402
- Frenzied behavior, 318
- Freon, 377
- Fresh water, 99
- Fresh whole blood transfusion for
 postpartum hemorrhage, 329
- Friction burns, management of, 224
- Frog corium, 532
- Frog support pad, 531
- Front foot, radiography of, 497, 498
- Front leg high suspensory disease (HSD),
 498
- Frontal nerve block (sensory) for lavage
 tubing installation, 459
- Frontal sinus, 369
 flexible endoscopy of, 372f, 373f
 portals for, 372
- Frozen semen
 extender of, 270
 for artificial insemination
 dosage of, 275
 protocol for, 276t
 postthaw, motility of, 269
 pregnancy rates from, 274t
 program for, 241-242
- Fructooligosaccharides, 714
- FSH. *See* Follicle stimulating hormone
 (FSH)
- 5-FU. *See* 5-fluorouracil (5-FU)
- Full bar shoe, 531f
- Full hindlimb bandage, 548f
- Full limb
 bandaging of, 548
 cast for, 549, 550
- Full-thickness burns, 222
- Fulminant hepatic failure, treatment of,
 172
- Fundus
 direct ophthalmoscopy of, 450-451
 examination of, 453-454
 indirect ophthalmoscopy of, 451
 zones of, 454
- Fungal agents causing interstitial
 pneumonia, 425
- Fungal conjunctivitis, 474
- Fungal cultures for eyelid lacerations, 464
- Fungal granulomas, 374
- Fungal hyphae, detection of, 466
- Fungal infections associated with
 ulcerative keratitis, 466
- Fungal keratitis, 451, 477-479
 clinical signs of, 477-478
 diagnosis of, 478
 incidence of, 477
 treatment of, 478-479
- Fungal uterine infections, 231
- Fungi, 197
- Fungicidal therapy for folliculitis, 200
- Fungizone. *See* Amphotericin B
 (Fungizone)
- Furacin for upper respiratory tract
 postoperative management, 395
- Furosemide
 for acute renal failure, 843
 for cerebrocortical edema, 770t
 for congestive heart failure, 617, 621
 for exercise-induced pulmonary
 hemorrhage, 432
 for forebrain disease, 770
 for negative-pressure pulmonary
 edema, 393
 for perinatal asphyxia syndrome, 648t
 for postpartum hemorrhage, 330
 for vasculitis, 365
- Fusarium*, 477, 792
- Fusarium moniliforme*, 765
- Fusion failure, 827-828
- Fusobacterium*, 6
- FWEC. *See* Fecal worm egg counts
 (FWEC)
- G**
- GAD. *See* Glutamic acid decarboxylase
 (GAD)
- GAGs. *See* Glycosaminoglycans (GAGs)

- Gait abnormalities, video recording of, 499
 Gait analysis, 735
 Beta-galactosidase (Lactase), 677
 Galloping in prepurchase examination, 497
Gambusia, 194
 Gamete intrafallopian transfer (GIFT), 285
 GAMMA-CHECK-E. *See* Glutaraldehyde clot test (GAMMA-CHECK-E)
 Gamma-glutamyl transferase (GGT), 169, 176, 821
 Gamma-oryzanol, 29
 Gammopathy, 360-361
 Ganglion cells, 456
 Gas chromatography, 33
 Gas chromatography/mass spectrometry (GC/MS)
 in drug testing, 33
 Gas colic, treatment of, 115
 Gas exchange, maintaining in foal pneumonia, 672-673
Gasterophilus, 194
 Gastric distention, cause of, 115
 Gastric outflow obstruction, in foals, 101-103
 clinical signs of, 101-102
 diagnosis of, 102-103
 treatment of, 103
 Gastric peristalsis, 101
 Gastric ulcers, 95-96
 neonatal, 5
 Gastroduodenal ulcer syndrome (GDUD), 101
 with viral enteritis, 680
 Gastroduodenojejunitis, 120
 GastroGard for gastric ulcers, 98
 Gastrointestinal disease, nutritional therapy for, 722-726
 Gastrointestinal motility, physiology of, 109
Gastrophilus, 163
 Gastrosocopy of foals, 685
 Gatifloxacin, 6
 GC/MS. *See* Gas chromatography/mass spectrometry (GC/MS)
 GCT. *See* Granulosa cell tumors (GCT)
 GDUD. *See* Gastroduodenal ulcer syndrome (GDUD)
 Gelatinases, 517
 Geldings, residual stallionlike behavior in, 319
 General anesthesia for foals, 687-691
 Generalized lymphoma, 359
 Generalized postanesthetic myopathy, differentiation of, 743t
 Generally regarded as safe (GRAS), 713
 Genetic predisposition to cervical stenotic myelopathy, 747
 Genetically superior mares, embryo transfers in, 277
 Genital tract, examination of for embryo transfers, 277
 Genitalia, examination of in recipient mares, 278
 Gentamicin, 6, 851
 dosage optimization of, 9
 dosing regimen, 852t
 for arytoid chondrosis, 382
 for *Clostridium difficile* infection, 168
 for duodenitis-proximal jejunitis, 123
 for foal pneumonia, 671
 for neonatal septicemia, 3, 660, 661t
 for ocular emergencies, 463t
 for peritonitis, 156
 for pleuropneumonia, 424
 Gentamicin—cont'd
 for rectal tears, 152
 for uroperitoneum, 858
 plasma concentration monitoring, 853f
Geotrichum, 477
 Gestational age, calculation of, 642
 Gestational length and readiness for birth, 315
 GGT. *See* Gamma-glutamyl transferase (GGT)
Giardia with foal diarrhea, 678
 GIFT. *See* Gamete intrafallopian transfer (GIFT)
 Glaucoma, 466
 clinical signs of, 486-487
 diagnosis of, 486-487
 etiology of, 486
 risk factors of, 486
 treatment of, 487-488, 487t
 Globe, 462-464
 rupture of, 464
 visual assessment of, 462
 Globe proptosis, blunt head trauma, 464
 Globule leukocyte, 410
 Glomerular filtration rate, measurement of, 823-824
 Glucocorticoids
 for acute respiratory distress syndrome, 676
 for arthropod hypersensitivity, 185
 for cervical stenotic myelopathy, 748
 for cutaneous lymphosarcoma, 210
 for pemphigus foliaceus, 218
 for vasculitis, 365
 for viral encephalitis, 770
 prior to *Culicoides* sensitivity test, 184
 Glucosamine, 26, 27, 570
 Glucose, 789
 and premature foals, 643
 Glucose intolerance, 814
 Glucose substrates for spermatozoa, 267
 Glucotoxicity, 813
 Glutamate, 645
 Glutamate dehydrogenase, 176
 Glutamic acid decarboxylase (GAD), 762
 Glutamine in parenteral nutrition, 113
 Glutamyl transferase, 58, 169, 176, 821
 Glutaraldehyde clot test (GAMMA-CHECK-E), 694
 Glutathione, 802
 Gluteal myositis, 495
 Gluteal tendinitis, 495
 Glycerol
 for cryopreservation, 282-283
 for parenteral nutrition, 112-113
 Glycogen as energy source, 112
 Glycopyrrrolate
 for dysrhythmias, doses of, 604t
 for foals, 691
 Glycosaminoglycans (GAGs), 477
 Glycosuria, 829
 GnRH. *See* Gonadotrophin-releasing hormone (GnRH)
 Goblet cells, metaplasia of, 414
 Gokel's operation, 834
 for cystic calculi, 833
 Gonadal hypoplasia in breeding mares, 261
 Gonadotrophin-releasing hormone (GnRH)
 during artificial insemination, 278
 during vernal transition, 239
 for inadequate libido, 317-318
 for oocyte transfer, 285-286
 for ovulation induction, 241
 Gonadotrophin-releasing hormone (GnRH)—cont'd
 frozen semen program, 241-242
 in cooled-transported semen program, 241
 Gradient echo imaging, 509
 Grain meal, 702
 Gram-negative infection, 105
 Gram's stain, 408
 Grand prix jumpers, distal hock joints soreness in, 499
 Granulation tissue complicating arytoidectomy, 383
 Granulomatous enteritis, 144-146
 clinical signs of, 145t
 Granulomatous mural folliculitis, 216
 Granulosa cell tumors (GCT)
 in mares
 hormonal concentrations in, 263t
 removal of, 262f
 ultrasonic image of, 262f
 with enlarged ovaries, 261-262
 Granulosa cells, 261
 Grapes, 201-203
 GRAS. *See* Generally regarded as safe (GRAS)
 Grass gruel for myasthenia, 745
 Grass hay, mineral content of, 721t
 Grease heel, 201-203
 Greater trochanter, palpation of, 496
 Green blow flies, 194
 Griseofulvin for sporotrichosis, 214
 Grooming soaps, causing corneal ulcers, 466
 Groundsel, 789
 Group A rotavirus, 679
 Growth hormone in aerosol, 437
 GsMtx-4 for atrial fibrillation, 608
 Guaifenesin, 19, 460
 for foal pneumonia, 672
 Guanidine chloride, avoidance of, 745
 Guarded culture instruments, 229
 Guarded scalpel, 320
 Gull wing lesion, 498
 Guttural pouch
 examination of, 368
 resembling progressive ethmoid hematoma
 mycosis of, 375
 neoplasms of, 375
 Guttural pouch disease, 386-390, 775
 Guttural pouch empyema, 65, 386-388
 treatment of, 67-68
 Guttural pouch mycosis, 388-390, 792
 treatment of, 389-390
 Guttural pouch openings, 384
 Guttural pouch tympany, 388
H
 HA. *See* Hyaluronic acid (HA)
Habronema, 195-197, 305, 474, 767
Habronema larvae, 196
Habronema majus, 195
Habronema microstoma, 195
Habronema muscae, 195
 Hackney horse, 384
 Hackney pony with dropped elbow, 736
Haematobia irritans, 184, 186, 193-194
 HAI. *See* Hemagglutination inhibition (HAI)
 Hair, removal of, 199
 Hairly vetch, 784
 Half-limb cast, 549f
Halicephalobus gingivalis, 767, 775
 Halogen light source, 366, 374

- Halothane for foals, 690
 Ham's F-10, 281-282
 Handler, aggressive behavior towards, 262
 Hand-walking for vasculitis, 365
Hansenula, 792
 Hanta virus causing interstitial pneumonia, 426
Haplopappus, 783
 Hard ticks, 189
 Harness, proper fit of, 570
 Hartman's solution, 222
 Harvest mites, 188
 Hawaii, poisonous plants in, 426
 Hay
 affecting heaves, 420
 feed-related toxicoses, 779
 for Quarter Horse-related breeds with polysaccharide storage myopathy, 733
 good quality, 705
 mineral content of, 721t
 silage, 420
 HCG. *See* Human chorionic gonadotropin (hCG)
 Head
 computed tomography of, 371f, 507
 trauma of, 774
 visual assessment of, 462
 Health certificate, requirements for semen shipment, 266
 Health regulations for semen shipment, 266
 Healthy horses, differential cell counts in, 409
 Heart
 dimensions of, 584t
 ice-pick evaluation of, 579
 normal development of, 591-592
 Heart murmurs. *See* Murmurs
 Heart rate, 586
 calculation of, 577
 of fetus, 632
 Heart sounds, 575-576
 Heart-bar shoe, 525
 Heat over legs, 503
 Heaves, 181, 417-421
 acute episodes of, 417-420
 bronchodilating agents for, 437
 definition of, 412
 exacerbation of, prevention of, 420-421
 medications for, 418t
 remission of, 420
 Heaves syndrome, 411
 Heavy metal intoxication, 620
 Heinz bodies, 344
Helicobacter pylori, 95
Heliotropium, 768, 788, 789
 Helminth parasites, 678
 Hemacytometer for sperm concentration determination, 267
 Hemagglutination inhibition (HAI), 44
 Hemagglutinin, 42
 Hemarthrosis
 iatrogenic, 15
 Hematocele in vagina, 306
 Hematocrit with anemia, 337
 Hematocyst, definition of, 306
 Hematoma with enlarged ovaries, 261
 Hematuria, 854-856
 Hemicellulose, 698
 Hemoconcentration, 358
 Hemolysins, testing for, 355
 Hemolytic anemia, 344-348
 diagnosis of, 338
 Hemolytic test, 637
 Hemophilia A (Factor VIII deficiency), 351
 Hemorrhage, 465
 clinical significance of, 340
 complicating surgical ablation of progressive ethmoid hematoma, 376
 diagnosis of, 352f
 of internal carotid artery, 389
 Hemorrhagic discharge, 491
 Hemorrhagic enteritis
 with *Clostridium difficile* infection, 167
 Hemorrhagic fibrinonecrotic duodenitis-proximal jejunitis, 120
 Hemorrhagic follicles, 261
 Hemosiderophages, 429
 Hemospermia, 255, 306
 Hemostatic agents, 21-22
 Hemostatic disorders, 351-354
 clinical signs of, 351
 Hemothorax, 434
 Heparin
 for disseminated intravascular coagulation, 354
 for thromboembolism, 627-628
 Hepatic disease, 717-718
 systemic signs of, 176
 Hepatic encephalopathy, 718
 associated with signs of forebrain disease, 765
 Hepatic failure, therapy of, 172
 Herbal treatments
 for equine recurrent uveitis, 470
 for musculoskeletal disorders, 570
 Hernias of abdominal wall, 310-311
 Herpes viruses, bronchoalveolar lavage, 411
 Herpesvirus keratitis, 478
 Herpesvirus keratoconjunctivitis, exacerbation of, 475
 Herpetic conjunctivitis, clinical signs of, 473-474
 Herpetic keratitis, 475
 Hespan. *See* Hydroxyethyl starch (Hespan)
 Hetastarch, 357
 for *Clostridium difficile* infection, 168
 for dehydration, 119
 Heterochromia iridis, 453
 Hexacetone, 552
 HGE. *See* Human granulocytic ehrlichiosis (HGE)
 HIE. *See* Hypoxic ischemic encephalopathy (HIE)
 High ambient temperature, 831
 High fat diet, 569
 High performance liquid chromatography (HPLC), ergopeptine alkaloid concentrations, 797
 High potassium diet precipitating hyperkalemic periodic paralysis, 721
 Hind fetlock, radiography of, 498
 Hind leg retraction test, 497
 Hindlimbs
 ankylosis of transverse presentation with, 321
 examination of, 496
 flexed at hocks, 321
 flexion of, 321, 497
 Hinged splints for incomplete ossification of cuboidal bones, 664
 Hip lock, 320
 Histamine, 407
 Histiolympocytic lymphosarcoma, 209
Histoplasma causing interstitial pneumonia, 426
 Hoary alyssum, 779
 Hoary false alyssum, 787
 Hock radiography of, 498
 Holosystolic murmur, 595f
 Holter monitor. *See* Resting 24-hour continuous electrocardiograms (Holter monitor)
 Holter monitoring, 572, 587, 602
 for atrial fibrillation, 608
 for ventricular ectopy, 610-611
 Honking musical murmurs, 615
 Hoofs
 care of, 470
 growth of, 520
 trimming of, 530-531
 wall resection, 527-528
 Hooks, 83-84
 Hoop capsule, stabilization of, 522
 Horay alyssum, 787
 Horizontal air artifacts in pneumothorax, 434
 Hormonal therapy
 causing estrus onset delay, 249-250
 for recipient mares, 279
 Horn flies, 186, 193-194
 Horner's syndrome, 389, 746
 Horse bots, 194-195
 Horse flies, 46, 184, 186, 191
 Host
 natural immunity, 477
 resistance, 23-24
 Hound's tongue, 789
 House flies, 194, 305
 Howell Jolly bodies, 337
 Ho:YAG laser for cystic calculi, 834
 HPA. *See* Hypothalamic-pituitary axis (HPA)
 HPLC. *See* High performance liquid chromatography (HPLC)
 HPT. *See* Hypothalamic-pituitary-testicular (HPT)
 H2-receptor antagonists for gastric ulcers, 98
 HuINF alpha. *See* Human interferon alpha (HuINF alpha)
 Human cardiopulmonary resuscitation, new directions in, 655
 Human chorionic gonadotropin (hCG)
 challenge with, in subfertile stallions, 259
 during artificial insemination, 278
 for artificial insemination preparation, 272-273
 for ovulation induction, 240-241
 frozen semen program, 241-242
 in cooled-transported semen program, 241
 Human granulocytic ehrlichiosis (HGE), 78, 348
 Human interferon alpha (HuINF alpha)
 for upper airway disease, 399
 Humidity control for interstitial pneumonia, 428
 Humorsol. *See* Demecarium bromide (Humorsol)
 Hunters
 navicular pain in, 498
 prepurchase examination of, 493
 Hurdle racing, 429
 Hyaline membrane disease, 643

- Hyaluronan, 519. *See* Sodium hyaluronate (hyaluronan)
- Hyaluronic acid (HA), 14-16, 519
commercially available preparations of, 556t
with corticosteroids, 15
- Hydralazine for afterload reduction, 621
- Hydration
assessment of, 117
of colic in foals, 681
- Hydroallantois, 301-302
with placental hydrops, 302
- Hydrocele in vagina, 306-307
- Hydrocephalus, 767
- Hydrochloric acid, 95
- Hydrofluoroalkane-134a, 437
- Hydrogel, 223
- Hydrogen peroxide, 25
formation of, 136
- Hydrolysable carbohydrates, 698
- Hydroponic hay, 420
- Hydrops allantois, 645
- Hydrops amnii, 632, 645
- Hydrotherapy
for alsike clover poisoning, 791
for vasculitis, 365
- Beta-hydroxy beta-methylbutyrate, 28
- Hydroxyethyl starch (Hespan)
for acute blood loss, 341
for salmonellosis, 59
- Hydroxyurea for polycythemia, 358
- Hydroxyzine
for arthropod hypersensitivity, 185
for atopic dermatitis, 183
for urticaria, 206
- Hyoscine for dysrhythmias, 604t
- Hyperadrenocorticism, 717
- Hyperbilirubinemia with anemia, 338
- Hypercalcemia, 846
- Hypericum*, 174
- Hyperechogenic allantoic fluid, 301
- Hyperfibrinogenemia, 61
- Hyperglycemia, 829
- Hyperimmune plasma
for equine viral arteritis, 38
for foal pneumonia, 674
for perinatal asphyxia syndrome, 648t
for peritonitis, 156
for retained fetal membranes, 332
- Hyperimmune serum
for endotoxin, 21
for small intestine strangulating obstruction, 124
- Hyperinsulinemia, 814
- Hyperkalemia, 223, 857
- Hyperkalemic periodic paralysis, 721-722
- Hyperkalemic periodic paresis, 743t
- Hyperlipemia, 716-717
in ponies, 701
therapeutics for, 22-23
- Hyperlipidemia, 22-23
- Hypersensitivity reactions causing
interstitial pneumonia, 426-427
- Hyperthermia for equine sarcoid, 205
- Hyperthyroidism, 250
- Hypertonic saline for dehydration, 156
- Hypertonic saline solution
for acute blood loss, 341
for postpartum hemorrhage, 329
for shock, 119
- Hypertonicity, 569
- Hypertriglyceridemia, 717
- Hypervolemia, phlebotomy for, 433
- Hyphema, 466
- Hypoalbuminemia, 144, 361
treatment of, 168, 172
- Hypochoeris radicata*, 739, 761
- Hypochloremia, 820, 841
- Hypochlorite disinfectants, 25
- Hypoderma*, 767, 775
- Hypoderma bovis*, 194
- Hypoderma lineatum*, 194
- Hypofibrinogenemia, 353
- Hypoglycemia, treatment of, 172
- Hypomagnesemia, 119
- Hyponatremia, 820, 841, 857
- Hypoproteinemia, 149
plasma infusion for, 143
with proliferative enteropathy, 165
- Hyposensitization
for arthropod hypersensitivity, 185
for atopic dermatitis, 183
- Hypothalamic-pituitary axis (HPA),
dopamine effect on, 239
- Hypothalamic-pituitary-testicular (HPT) axis, 257
diagnostic evaluation of, 257-258
of stallion, 258f
- Hypothalamus, 764
- Hypothermia, 681
in foals, 688
- Hypothermia in human cardiopulmonary resuscitation, 655
- Hypothyroid, 806
- Hypothyroidism, 715
and infertility, 250-251
clinical signs of, 251
diagnosis of, 250
- Hypovolemic shock
determination of, 657
signs of, 336
- Hypoxemia in septic foals, 657
- Hypoxia, 645-646, 646
- Hypoxic ischemic encephalopathy (HIE),
632, 644, 655, 767, 775-776
in neonatal foal, 633-634
- I**
- Iatrogenic burns, 222
- Iatrogenic hemarthrosis, 15
- Ice-pick evaluation, 579
- Icterus, 336
- Idiopathic eosinophilic enterocolitis, 147
- Idiopathic inflammatory bowel disease, 146t
- Idiopathic interstitial pneumonia
caudodorsal lung field in
radiographic appearance of, 427f
- Idiopathic postanesthetic myasthenia syndrome, 740
- Idiopathic renal hematuria, 855-856
- Idiopathic synovitis
atropine for, 557
- Idoxuridine for herpetic keratitis, 475
- IgE. *See* Immunoglobulin E (IgE)
- IgG. *See* Immunoglobulin G (IgG)
- IgG blood level in foals, 323
- IgM. *See* Immunoglobulin M (IgM)
- IL-1. *See* Interleukin-1 (IL-1)
- IL-6. *See* Interleukin-6 (IL-6)
- Ileal impaction, 127-130
clinical signs of, 128
diagnosis of, 128
during exploratory celiotomy, 130f
etiology of, 127-128
prevalence of, 127
prognosis of, 130
treatment of, 128-129
vs. strangulating obstructions, 127
- Ileal impaction colic, prevention of, 160
- Ileal orifice, 127
- Ileocecal intussusception, abdominal
ultrasonography of, 682f
- Ileocecal junction, 127
- Ileocolic artery, anatomy and physiology
of, 138
- Ileus, 108-111, 648
anatomy and physiology of, 127
clinical signs of, 109
diagnosis of, 109
prokinetic agents for, 22t
prokinetic drugs for, 109-111
treatment of, 109
- Iliac artery, rupture of, 327
- Illuminance, 238
examples of, 239t
- Illumination, calculation of, 238
- Imaging in prepurchase examination,
497-498
- Imaverol. *See* Enilconazole (Imaverol)
- Imidocarb dipropionate for
piroplasmiasis, 348
- Imipenem for neonatal septicemia, 4
- Imipramine for ejaculation dysfunction,
318
- Immediate postpartum period, signs of
problems during, 633
- Immune modulator therapy for lower
motor neuron disease, 752
- Immune therapy for neonatal septicemia,
659-660
- Immune-mediated hemolytic anemia,
345
diagnosis of, 360
- Immune-stimulating complexes
(ISCOMs), 43
- Immunity in neonates, 692
- Immunization for endotoxemia, 106
- Immunoblots for equine protozoal
myeloencephalitis, 71
- Immunodeficiencies
acquired, 696
in foals, 696-697
in vitro immunologic testing for,
446b
of foals, 692-699
- Immunoglobulin E (IgE), 184
- Immunoglobulin G (IgG), 52, 218
index, 72
measurement of, 694
- Immunoglobulin in colostral immunity,
692-693
- Immunoglobulin M (IgM), 52, 361
- Immunoglobulin therapy for
thrombocytopenia, 350
- Immunoglobulins, blocking ocular
infection, 477
- Immunohistochemistry, 218
- Immunomodulators, 446t
in respiratory disease treatment, 445-448
- Immunophenotyping for cutaneous
lymphosarcoma, 210
- Immunosuppression
in selenium intoxication, 803
with mold infection, 793
- Immunosuppressive glucocorticoid
therapy for lymphoma, 361
- Immunotherapy
for equine sarcoid, 205
for foal pneumonia, 673
for sarcoid, 485
- Impacted meconium, of foals, abdominal
radiography of, 683f

- Impinged spinous process, 570
 - management of, 571
 - nuclear scintigraphy of, 501
- Implant gun, 283, 284f
- In utero growth retardation (IUGR), 645
- Inactivated vaccines for rabies, 770-771
- Inadequate erythropoiesis, 337, 339
 - anemia secondary to, 342-343
- Inadequate libido of stallions, 317-318
- Incisor malocclusions, 87f
- Incisors, 86-87
- Incontinence, surgery of, 327
- Increased radiopharmaceutical uptake (IRU), 500-501
- Indiana hemp, 783
- Indiana vesicular stomatitis virus (VSV-Indiana), 51
- Indirect fluorescent antibody for equine monocytic Ehrlichiosis, 76
- Indirect ophthalmoscopy, 451
- Indocyanine green test, 170
- Indolent ulcer, 478
- Indwelling chest tubes, 423
 - for pleural effusion drainage, 423
- Infection triads, disrupting, 23
- Infectious agents causing interstitial pneumonia, 425-426
- Infectious disease, preventing spread of, 23-26
- Inferior check ligament, desmitis in, 499
- Infertility
 - and embryo recovery, 277
 - and hypothyroidism, 250-251
 - cause of, 231
- Infiltrative bowel diseases, 144-147
- Inflammatory airway disease, 407
 - clinical signs of, 412-413
 - definition of, 412
 - demeanor change with, 416
 - functional disturbances associated with, 414
 - in non-racehorses with cough, 416
 - in performance horse, 412-417
 - infection as risk factor for, 414
- Inflammatory bowel disease
 - idiopathic, 146t
 - microscopic lesions in, 146t
- Inflammatory mediators
 - in ischemia-reperfusion injury, 136
 - mast cells releasing, 413
- Inflammatory upper airway disease and muscle dysfunction, 398-399
- Influenza vaccine, 252
 - bronchoalveolar lavage, 411
- Infrared radiation detector, 502
- Infusion pipette, 227
- Infusion pump for parenteral nutrition, 114
- Ingested chemicals causing interstitial pneumonia, 426
- Inguinal hernia, 149, 307
 - examination for, 306
- Inguinal rings, examination of, 306
- Inhalation therapy, 437
- Inhalational anesthesia for foals, 689, 690
- Inhaled chemicals causing interstitial pneumonia, 426
- Inhaled corticosteroids
 - for heaves, 418-419
 - for internal airway disease, 442
 - for recurrent airway obstruction, 442-443
 - stepwise, 443
 - short-term administration of, 419
- Inherited coagulation disorders, 351
- Inhibin, 257
 - in subfertile stallions, 258
 - production of, 261
- Injectable anesthetics
 - for foals, 689-690
 - protocols for, 17-19
- Injured penis, support of, 304f
- Inlet ventricular septal defects (VSD), 596
- Inner catheter within 8 French guiding catheter, 402
- Innervation, autonomous zones of, 738f
- Insect hypersensitivity, 184
- Insecticides, 193b, 770
 - causing corneal ulcers, 466
- Insemination
 - dose for, 268
 - protocols for, 241b-242b
- Inseminator, 273
- Insidious equine recurrent uveitis (ERU), 468-469
- Inspiratory noise, abnormal, 383
- Insulin
 - in aerosol, 437
 - insensitivity
 - endothelial cell dysfunction, 813
 - stress, 813
 - refractory state, 812-813
 - obesity, 812-813
- Insurance for breeding stallions, 253
- Intal. *See* Sodium cromoglycate (Intal)
- INTEGRA, 223
- Intentional iatrogenic burns, 221
- Interactive bonding behavior between foal and mare, 264
- Interferon alpha for respiratory disease, 39, 448
- Interferon alpha-2a (Roferon), 448
- Interferons, 445
 - for upper airway disease, 399
- Interleukin-1 (IL-1), 445, 553
- Interleukin-6 (IL-6), 445
- Intermittent arrhythmias, recording of, 577
- Intermittent pericardiocentesis, 623
- Internal burns, 224
- Internal carotid artery
 - hemorrhage of, 389
 - ligation of, 390
- Interphalangeal joints, flexion of, 497
- Interstitial brachytherapy for sarcoid, 485
- Interstitial cell tumors of testicles, 308
- Interstitial pneumonia, 425-429
 - causes of, 425b
 - clinical signs of, 427
 - diagnosis, 427-428
 - etiology of, 425-426
 - idiopathic, caudodorsal lung field in, 427f
 - pathophysiology of, 427
 - postmortem histopathology of, 428f
 - prognosis of, 428-429
 - treatment of, 428
- Intestinal adhesions, 155
- Intestinal epithelium as barrier to pathogenic microorganisms, 114-115
- Intestinal motility, modulation of, 108-111
- Intestinal myoelectric activity, 139
- Intestinal rupture. *treatment of*, 155
- Intestinal tapeworm, 158-160
 - coprologic diagnosis of, 158-159
 - epidemiology of, 158
 - investigation of, 158-159
 - prevention of, 160
 - treatment of, 159-160
- Intestinal viability, assessment of, 137
- Intestinal volvulus, 681
 - abdominal radiography of, 683f
 - abdominal ultrasonography, 682f
- Intraabdominal abscess, *treatment of*, 157
- Intraabdominal adhesions, *formation of*, 126f
- Intraarticular atropine, 557
- Intraarticular blocks, 500
- Intraarticular corticosteroids, 551-554
 - equine studies of, 552-553
 - for competing horses
 - regulatory issues associated with, 554
 - pharmacology of, 551-552
 - recommended doses of, 553-554
- Intraarticular glycosaminoglycans (GAGs), 556
- Intraarticular hyaluronan, 555-556
- Intraarticular pentosan polysulfate (PPS), 557
- Intraarticular polysulfated glycosaminoglycans (PSGAGs), 556-557
- Intraarticular superoxide dismutase, 557
- Intracamerai injection, 460
- Intracranial abscesses, 770
- Intradermal allergy test, 181-182
- Intralesional chemotherapy, 483
- Intralesional therapy, 460
- Intranasal humidified oxygen for perinatal asphyxia syndrome, 648t
- Intraocular pressure (IOP)
 - and aqueous humor, 486
 - estimation of, 462
 - measurement of, 474
- Intravascular hemolysis
 - acute, 338
 - diseases causing, 344-345
- Intravenous fluid therapy for dehydration, 118-119
- Intraventricular septum,
 - echocardiography of, 582f
- Intravitreal cyclosporine A devices (IVC-As), 472t
 - for equine recurrent uveitis, 470
- Introducer catheter-over-needle flushing catheter, 402
- Intussusception of small intestine, 149
- Iodide
 - for foal pneumonia, 672
 - for sporotrichosis, 214
 - toxicity of, 214
- Iodine for upward fixation of the patella, 536
- Ionic cathartics for large colon impaction, 133
- Ionophore toxicity
 - acute, differentiation of, 743t
 - treatment of, 745
- IOP. *See* Intraocular pressure (IOP)
- Ipratropium bromide
 - for heaves, 419
 - for interstitial pneumonia, 428
 - hydrofluoroalkane-134a formulation of, 437
- Iridocorneal angle, 467
 - slit lamp biomicroscope examination of, 450
- Iridocyclitis, 458, 462, 465, 466, 474
 - treatment of, 466
- Iris
 - examination of, 453
 - multiple colors within, 453

Iris—cont'd
 prolapse of, 466, 479
 fungal infection associated with, 466
 slit lamp biomicroscope examination of, 450
 Iron fumarate toxicity, 171
 Iron metabolism in foals, 343
 Iron supplements, oral administration of, 7
 Iron-deficiency anemia, 342-343
 Irreducible paraphimosis, 303
 IRU. *See* Increased radiopharmaceutical uptake (IRU)
 Ischemia
 adenosine triphosphate during, 135
 in premature foals, 634
 Ischemia-reperfusion injury, neutrophils in, 136
 ISCOMs. *See* Immune-stimulating complexes (ISCOMs)
 Isoenzyme 5 of lactate dehydrogenase (LDH-5), 169
 Isoflupredone acetate for heaves, 418
 Isoflurane for foals, 690
 Isolation, 24-25
 Isotonic fluids, 119
 for negative-pressure pulmonary edema, 393
 for small intestine strangulating obstruction, 124
 Isotonic polyionic fluids for shock, 107
 Isoxsuprine
 for long breakover, 534
 for placental hydrops, 302
 Itraconazole (Sporanox), 479t
 for guttural pouch mycosis, 389
 for ocular emergencies, 463t
 IUGR. *See* In utero growth retardation (IUGR)
 IVC-As. *See* Intravitreal cyclosporine A devices (IVC-As)
 Ivermectin
 cyathostomiasis resistance to, 162-163
 for brainstem disease, 777
 for cutaneous habronemiasis, 305
 for cyathostomes, 162
 for intestinal tapeworm, 159
 for mite control, 190
 for skin parasites, 196
Ixodes, 54, 55f
Ixodes holocyclus, 740
Ixodes pacificus. *See* Western black-legged tick (*Ixodes pacificus*)
Ixodes scapularis. *See* Deer tick (*Ixodes scapularis*)
 Ixodid ticks, 189
J
 Jamestown Canyon virus, 52, 88
 Japanese B encephalitis, 766
 Japanese encephalitis, 50
 Jaundice foal agglutination test, 637, 637t
 Jejunocecostomy, preventing reimpaction of ileum, 130
 Jejunum, lipoma strangulation of, 125f
 Jet nebulizers, 439
 Jimmyweed, 783
 Joint disease
 biomarkers of, 513-520
 nonsteroidal antiinflammatory drugs for, 558-559
 pathobiology of, 558
 systemic therapy, 558-561
 treatment of, 558
 Joint effusion in neonates, 657

Joint injury, postoperative management of, 545-546
 Joint stiffness, manual therapy of, 567
 Joint tissue metabolism, biomarker assays of, 516t
 Joints, soft tissue injuries around, magnetic resonance imaging of, 509
Juga yrekaen. *See* Snail (*Juga yrekaen*)
 Jugular veins
 catheterization of, 329
 disease effect on, 574
 distention of, 573-574
 examination of, 384, 573-574
 normal pulsations of, 574
 thrombophlebitis/thrombosis, 625-626
 Jumpers
 carpal joint disease in, 498
 inferior check ligament desmitis in, 499
 prepurchase examination of, 493
 with front leg high suspensory disease, 498
 Junctional epidermolysis bullosa, 219
K
 Kalayjian swab, 226-227
Kalmia, 783
 Karo syrup for hepatic failure, 172
Karwinskia humboldtiana, 783-784
 Kauffmann-White scheme, 56
 KCS. *See* Keratoconjunctivitis sicca (KCS)
 Kenney semen extender, formula for, 270b
 Keratan sulfate, 515
 Keratinocytes, 803
 proliferation of, 480
 Keratitis, 462, 465
 clinical signs of, 475
 Keratoconjunctivitis sicca (KCS), 474
 secondary to neurologic disease, 476
 Keratomycosis, 466
 Kernicterus, 636
 Ketamine, 18, 19
 for bilateral laryngeal paralysis, 392
 for foals, 689
 Ketoconazole (Nizoral), 479t
 Ketofen. *See* Ketoprofen (Ketofen)
 Ketoprofen (Ketofen)
 blocking leukotriene synthesis, 107
 for colic, 116
 for foals, 691
 for joint disease, 559
 for neonates, 4, 5
 for retained fetal membranes, 332
 Kicks received during breeding, 303
 Kidneys
 imaging of, 149, 823
 neoplasms of, 835
 Kimura platinum spatula, 478
 Kissing lesions, 381
Klebsiella, 10, 838
 in semen, 255
Klebsiella pneumoniae, 6, 11
 causing placatitis, 297
 causing retained fetal membranes, 330
 in foal pneumonia, 666
 in jugular vein thrombophlebitis, 626
 in thoroughbred racehorses, 414
Kluyveromyces fragilis, 711
 Krey-Schotter hook, 320
 Kyphosis, 495
L
 Laboratories for neonatal isoerythrolysis, 639t
 Lacrimal drainage, measurement of, 491
 Lacrimal sac, 489

Lacrimal system, examination of, 452
 Lacrimation, excessive, 462
 vs. epiphora, 489-490
 Beta-lactam antibiotics
 dosage optimization of, 9
 for neonatal septicemia, 3
 for peritonitis, 156
 neonatal volume of distribution, 3
 Lactase. *See* Beta-galactosidase (Lactase)
 Lactase supplementation for *Clostridium difficile* infection, 168
 Lactate dehydrogenase (LDH), 176, 744
 in stiff horse syndrome, 763
 Lactated Ringer's solution, 113, 222
 Lactation, failure of, 332
 Lactitol, 714
Lactobacillus agilis, 27
Lactobacillus bulgaricus, 712
Lactobacillus crispatus, 27
Lactobacillus plantarum, 27
Lactobacillus reuteri, 27
Lactobacillus salivarius, 27
 Lactoferrin
 blocking ocular infection, 477
 in colostrum, 692
 Lactose intolerance, 677
 Lactulose, 718
 for hepatic failure, 172
 Lamellae, separation of, 520
 Lameness
 diagnosis of, 500
 foot, proton density image of, 512f
 in neonates, 657
 in performance horse, treatment of, 559
 midpalmar pastern, T2-weighted image of, 510f
 navicular bone, proton density image of, 512f
 observation of, 497
 pastern, proton density image of, 510f
 trochlear ridge, fat-suppressed sagittal image of, 511f
 Laminitis, 77, 722
 chronic. *See* Chronic laminitis
 diagnosis of, 521
 etiology of, 702
 evaluation of, 521
 obesity, 813-814
 outcome of, 522
 presentation of, 521
 prognosis of, 522
 radiographic findings in, 521
 rehabilitation from, complications during, 521
 signs of, 361
 supportive therapy for, 522-523
 treatment of, 522
 with retained fetal membranes, 332
 Laparocystotomy for cystic calculi, 833
 Large (bronchi) airway obstruction vs. small (bronchiole) airway obstruction, 415
 Large colon
 dehydration of, 131
 displacement of, 149
 impaction of, 99, 131-135
 clinical signs of, 132-133
 epidemiology of, 131
 etiology of, 131
 prognosis of, 134-135
 rectal examination for, 132
 treatment of, 133-134
 nephrosplenic entrapment of, 149

- Large colon—cont'd
 reperfusion injury in, 136
 volvulus of, 135-137
- Laryngeal hemiplegia, 389, 416
 in non-racehorses, 383-386
 clinical significance of, 384-385
 clinical signs of, 384
 diagnosis of, 384
 treatment of, 385-386
- Laryngoplasty, 385
 for laryngeal hemiplegia, 385-386
- Laryngotomy approach for
 arytenoidectomy, 382
- Larynx
 examination of
 for laryngeal hemiplegia in non-racehorses, 384
 function of, 385
 neoplasms of resembling progressive ethmoid hematoma, 375
 stiffness of, 367-368
 ventricles of, 367
- Lasalocid intoxication, 620
- Laser ablation of progressive ethmoid hematoma, 377
- Laser fiber, 541f
- Laser light, components of, 393
- Laser lithotripsy
 disadvantages of, 834
 for cystic calculi, 833-834
- Laser puncture, 569
- Laser surgery of upper respiratory tract, 393-396
- Lasers
 characterization of, 393
 in respiratory surgery
 general use of, 394-395
 safety of, 395
- Lashes, 452
- L-asparaginase (Elspar)
 for cutaneous lymphosarcoma, 211
 for lymphoma, 361
- Late gestation
 placenta thickness during, 299f
 pregnancy loss during, 297
 uterus thickness during, 299f
- Late postoperative management
 of the orthopedic patient, 545-546
- Late-gestational mare
 transabdominal ultrasonographic image, 298f
 transrectal ultrasonography of, 299f
- Latex reservoir, 459
- Lavage
 for esophageal obstruction, 93
 for guttural pouch empyema, 387
- Lavage tubing
 installation of, 459
 retrograde placement of, 459
- Lawsonia intracellularis*, 164-166
 causing enteritis, 167
 in foal diarrhea, 679
- Laxatives
 for abdominal wall hernias, 310
 for rectal tears, 152
- LC/MS. *See* Liquid chromatography/mass spectrometry (LC/MS)
- LDH-1, 611
- Lead system, 576
- Left arm electrode, 602
- Left atrium, parasternal long axis
 reference view of, 584f
- Left basilar ejection murmur, 595
- Left ventricle
 dysrhythmias
 electrocardiogram, 587f
 echocardiography of, 582f
 M (motion) mode echocardiography, 621f
 short axis echocardiogram of, 582f
- Left ventricular outflow tract (LVOT)
 view, 580
- Left-to-right shunt, 594
- Legs
 heat over, 503
 mange of, 187
- Leishman's stain, 408
- Lens
 direct ophthalmoscopy of, 451
 emergencies involving, 466-467
 examination of, 453
 instability of
 cause of, 467
 opacity of, 450
 slit lamp biomicroscope examination of, 450
- Lens reflection, 453
- Lentiviruses, 45
- Leptoconops*, 191
- Leptospira*, 469
 uveitis, 468
- Leptospira icterohaemorrhagiae* causing
 intravascular hemolysis, 345
- Leptospira pomona* causing intravascular
 hemolysis, 345
- Lesions in prepurchase examination, 498
- Leucaena*, 215
- Leukemic phase of lymphoma, 359
- Leukeran. *See* Chlorambucil (Leukeran)
- Leukoencephalomalacia associated with
 signs of forebrain disease, 765-766
- Leukopenia, 105
- Leukotriene synthesis blocked by
 ketoprofen, 107
- Leukotrienes, 420
- Levamisole (Levasole)
 for equine protozoal myelitis, 754
 for lower motor neuron disease, 752
 for respiratory disease, 448
- Levothyroxine for anhidrosis, 817
- Leydig's cell tumors of testicles, 308
- LH. *See* Luteinizing hormone (LH)
- Lichenoid interface dermatitis, 179
- Lidocaine, 287
 for aortocardiac fistulas, 625
 for dysrhythmias, 604t
 for foals, 689
 for ileus, 111
 for ocular emergencies, 463t
 for ophthalmic examination, 451
 for shock, 107
 for transvaginal reduction, 247
 for ventricular tachydysrhythmias, 612
 in critical care, 20
- Ligament injuries
 postoperative management of, 546
- Light
 affecting spermatozoa, 266
 sensitivity to, 454-455
- Lightning strike, 774-775
- Light-shielded incubator, 267
- Lily of the valley, 783
- Limb ataxia, 773
- Limb deformities, angular. *See* Angular
 limb deformities
- Limb leads, 602
- Limb weakness, 773
- Limbal neoplasms, 480
- Limbal squamous cell carcinoma, 482-483
- Lime sulfur
 for equine pastern dermatitis, 202-203, 203
 for folliculitis, 200
 for mite control, 190
- Lincomycin, dosage optimization of, 9
- Lincosamides, dosage optimization of, 9
- Lindane for mite control, 190
- Line firing iatrogenic burns caused by, 222
- Linear alopecia, 216-217
- Linear array rectal transducer, 288
- Linear keratosis, 216-217
- Lipid solutions for neonatal septicemia, 662
- Lipids in parenteral nutrition, 112-113
- Lipoma, strangulating jejunum, 125f
- Lipoperoxidation, of cell membranes, 136
- Lipopolysaccharide (LPS), 104
- Lipoprotein lipase, in parenteral
 nutrition, 112-113
- Lipoproteins, protecting spermatozoa, 267
- Lipoxygenase-activating-proteins, 420
- Liquid chromatography/mass
 spectrometry (LC/MS) in drug
 testing, 33
- Liquid crystals, 502
- Liquid digesta, 127
- Liquid nitrogen
 for embryo storage, 281
 for semen freezing, 270-271
- Listeria monocytogenes*, 775
- Lite Salt, 817
- Liver
 imaging of, 148
 in foals, 688
 ultrasound of, 170
- Liver biopsy, 170-171
- Liver disease, 169-173
 diagnosis of, 169-170
 differential diagnosis of, 171-172, 171b
 therapy of, 172-173
- LMN. *See* Lower motor neuron (LMN)
- Local anesthetics
 for abdominal laparoscopy, 149
 in critical care, 20
- Lochia, 331
- Locoweed intoxication, 767
- Long axis echocardiogram, 581f
- Long bone, fractures of, postoperative
 management of, 546
- Long breakover
 diagnosis of, 532-533
 treatment of, 534
- Long teeth, 85, 85f
- Long-acting beta2-agonists for recurrent
 airway obstruction, 443-444
- Longissimus dorsi muscles, examination
 of, 496
- Longus capitis muscle, rupture of
 resembling progressive ethmoid
 hematoma, 375
- Loop colostomy, 152
- Loop snare, 321
- Lordosis, 310, 495
- Low flank approach for cesarean section, 322
- Low-DCAB diet, 719
- Lower airways
 disease
 controversy about, 412
 inflammation of, 413-414
- Lower eyelids, laceration of, 465
- Lower limb, bandaging of, 547-548

- Lower limb cast, 550
 Lower motor neuron (LMN)
 weakness, 571
 Lower motor neuron (LMN) disease, 735, 750
 causes of, 751t
 clinical signs of, 751-752
 diagnosis of, 752
 disorders causing, 741t
 treatment of, 752-753
 Low-molecular-weight heparin,
 antithrombotic effect of, 108
 Low-output cardiac failure, 574
 LPS. *See* Lipopolysaccharide (LPS)
 L-tryptophan for frenzied behavior, 318
 Luminous flux, 238
 Luminys Table, 505
 Lung abscesses, athletic horses with, 408
 Lung resection, 423
 Lung sounds in foal pneumonia, 669
 Lungs
 molds in, 792
 neoplasms of
 resembling progressive ethmoid
 hematoma, 375
 Lupus-erythematosus-like drug eruptions,
 histopathology of, 179
 Lush pastures causing laminitis, 702
 Luteinizing hormone (LH), 257
 for artificial insemination preparation,
 272
 in subfertile stallions
 diagnostic measurement of, 258
 temporal changes in, 259f
 Lux, 238
 LVOT view. *See* Left ventricular outflow
 tract (LVOT) view
 Lyme disease, 54-55, 775
 Lymphadenitis, 64
 Lymphocytes, 228
 in athletic horses, 409f
 in bronchoalveolar lavage, 409
 in cycling mare, 228
 in tracheal aspirates, 405
 Lymphocytic interstitial pneumonia,
 426-427
 Lymphocytic leukopenia with equine
 viral arteritis, 364
 Lymphocytic plasmacytic bronchitis,
 426-427
 Lymphocytic plasmacytic enterocolitis,
 146-147
 clinical signs of, 145t
 Lymphoma, 359-361
 alimentary type of, 359
 extranodal sites of, 360
 Lymphoproliferative disorders, 359-362
 Lymphosarcoma causing neoplastic
 effusions, 423-424
 Lymphosarcomas, 767
 with cauda equina, 758
 Lyons, John, 570
 Lyophilized immunoglobulin, 356
 Lyphomune, 356
 Lysergic acid, 796
 Lysergol, 796
 Beta lysin, blocking ocular infection, 477
- M**
 M (motion) mode echocardiography,
 578-579, 583f
 of left ventricle, 621f
 of mitral regurgitation, 616f
 of ventral septal defects, 598
 of ventricles, 615f
- MacConkey's agar, 229
 Macrolide antibiotics, oral administration
 of, 7
 Macrophages
 in athletic horses, 409f
 in tracheal aspirates, 404-405
 Macroscopic hematuria, 855
 Macrotube, 269-279
 Maedi-visna virus, 45
 Magnesium, 811
 for ECD, 717
 in feed, 721t
 Magnesium hydroxide for gastric ulcers,
 96
 Magnesium sulfate
 for aortocardiac fistulas, 625
 for dehydration, 119
 for dysrhythmias, 604t
 for large colon impaction, 133-134
 for perinatal asphyxia syndrome, 648t
 for ventricular tachydysrhythmias,
 612
 Magnesium-based laxatives, avoidance of,
 745
 Magnetic resonance imaging (MRI)
 clinical uses of, 508-513
 limitations of, 513
 of orthopedic disease, 509-510
 Magnetic transfer contrast imaging, 509
 Maiden mares, persistent mating-induced
 endometritis in, 235
 Mail-order semen, 268
 Main Drain virus, 766
 Malalignment ventricular septal defects
 (VSD), 596
 Malathion
 for equine pastern dermatitis, 203
 for mite control, 190
 Male fetus
 at 60 days
 ultrasound of, 289f, 290f
 tibia-tailhead triangle, 293
 Male gonads, distinguishing features of,
 293f
 Male tubercle, 293
 Malevolent sarcoids, 203
 Maltese cross, 348
 Mammary development and readiness for
 birth, 315
 Mane and tail dysplasia, 215
 Manganese, 26
 Mange, 187-188, 189
 Mange mites, 189
 identification of, 190
 Manipulation in prepurchase
 examination, 493
 Mannitol
 for acute renal failure, 843
 for cerebrocortical edema, 770t
 for forebrain disease, 770
 for negative-pressure pulmonary
 edema, 393
 for perinatal asphyxia syndrome, 648t
 for viral encephalitis, 770
Mansonella, 48
 Manual examination of perineal
 lacerations, 333
 Manual lithotrites for cystic calculi, 833
 Manual reduction, 245-246
 Manual therapy of musculoskeletal
 disorders, 567-568
 Manure, management of, 194
 MAP. *See* Mean arterial blood pressure
 (MAP)
 MAP-5 for racehorses, 555
- MAPC. *See* Migration action potential
 complex (MAPC)
 Mares
 aggressive behavior towards handler,
 262
 ambivalence towards foal, 264
 arterial rupture in, 327
 as candidates for foal heat-breeding,
 249
 avoiding foals, 265
 behavioral problems of, 264-265
 breeding of, time determination for,
 249-250
 care of after breeding, 250
 extreme protectiveness toward foal, 264
 fearing foal, 265
 granulosa cell tumors in
 hormonal concentrations in, 263t
 removal of, 262
 ultrasonic image of, 262f
 with enlarged ovaries, 261-262
 in transition, selection of, 278
 normal chromosomes number for, 261
 nursing avoidance of foal, 265
 preparation for artificial insemination,
 272-273
 reproductive tract of, examination of,
 272
 rolling for uterine torsion, 313
 savage attacks on foals, 265
 selection for breeding, 248-249
 stallionlike behavior of, 265
 stealing foals by, 265
 Margined beetles, 784
 Mass median aerodynamic diameter
 (MMAD), 437
 Mass spectrum, 33
 Massage, 569
 for myasthenia, 745
 for penile trauma, 303
 Mast cell blockers for heaves, 420-421
 Mast cell inhibitors for recurrent airway
 obstruction, 443
 Mast cells
 in bronchoalveolar lavage, 409
 in tracheal aspirates, 405
 releasing inflammatory mediators, 413
 Mastication muscles, atrophy of, 773
 Maternal readiness for birth, 315
 Maternal-foal behavior, 264
 Maternal-foal behavior, abnormal, 264-
 265
 Matrix metalloproteinases (MMPs), 515-
 516
 for cartilage degradation, 517
 Maxillary sinus, 369
 Maxillary vein, thrombus, ultrasound,
 626f
 Maxipime. *See* Cefepime (Maxipime)
 May Gruenwald stain, 408, 416
 McCullough swab, 226-227
 MCH. *See* Mean corpuscular hemoglobin
 (MCH)
 McMaster technique for fecal worm egg
 counts, 162
 MCV. *See* Mean corpuscular volume
 (MCV)
 MDI. *See* Metered-dose inhaler (MDI)
 MDP. *See* Methylene diphosphonate
 (MDP)
 M:E. *See* Myeloid to erythroid ratio (M:E)
 Mean arterial blood pressure (MAP) of
 foals, 687
 Mean corpuscular hemoglobin (MCH),
 337

- Mean corpuscular volume (MCV), 337, 340
- Mean heart rate of foals, 687
- Mechanical nebulizers, 439
- Meclofenamic acid (Arquel), 13
for joint disease, 559
- Meconium
composition of, 680-681
impaction
therapy for, 5
staining, 633
- Medial front splints, 498
- Medial malleolus lysis, cysts of,
computed tomography of, 507
- Medial septum, fenestration of, 388
- Mediastinal lymph nodes, lymphoma of,
359-360
- Medications
aerosolized for heaves, 420
authorized in racing, 34
- Medroxyprogesterone for endometrial
cysts, 232
- MEED. *See* Multisystemic eosinophilic
epitheliotropic disease (MEED)
- Megestrol acetate for cutaneous
lymphosarcoma, 211
- Meibomian (tarsal) glands, 452, 488
- Melanin, 174
- Melanoma in cranial mediastinum,
sonographic appearance of, 424f
- Melanosarcoma with cauda equina,
758
- Melphalan (Alkeran) for plasma cell
myeloma, 362
- Menace response, 452, 764
abnormal, 773
- Meningitis, 767
in septic foals, 657
- Meningoencephalitis complicating
surgical ablation of progressive
ethmoid hematoma, 377
- Mental depression in cranial nerve
diseases, 772
- Mephitis mephitis*. *See* Striped skunk
(*Mephitis mephitis*)
- Mepivacaine
detection of, 32
in critical care, 20
- Mercury toxicosis, 89-90
- Mesocolon, rupture of, effect on
peritoneal fluid, 296
- Metabisulphite, 437
- Metabolic acidosis
cause of, 119
in neonatal isoerythrolysis, 636-637
- Metabolic conditions, 715-722
causing interstitial pneumonia, 427
- Metabolic stress tests, 413
- Metabolic syndrome, 812
- Metacarpal region, computed
tomography of, 506, 507f
- Metacarpophalangeal joints, 497
radiography of, 497, 498
- Metacarpus, temperature of, 503
- Metathalamus, 764
- Metered-dose inhalant delivery devices,
438f
- Metered-dose inhalant systems, 437-439
- Metered-dose inhaler (MDI) cannister,
437
- Methasone
equine studies of, 552
for cutaneous lymphosarcoma, 210
recommended dosage of, 553
- Methemoglobin, 344
- Methyl sulfonyl methane for interstitial
pneumonia, 428
- Methyl-D-aspartate receptors, 645
- Methylene diphosphonate (MDP), 500
- Methylmethacrylate impregnated beads,
526
- Methylprednisolone acetate (Depo-
Medrol), 552
equine studies of, 552
in coffin joint, 556
- Methylprednisolone for cerebrocortical
edema, 770t
- Methylsulfonylmethane (MSM), 570
for exertional rhabdomyolysis, 730
- Methylxanthines, neonatal metabolism
of, 3
- Metoclopramide
for gastric flow obstruction, 103
for ileus, 110
for perinatal asphyxia syndrome, 648,
648t
- Metronidazole, 6, 770
for *Clostridium difficile* infection, 168
for hepatic failure, 172
for jugular vein thrombophlebitis, 626
for neonates, 4
for peritonitis, 156
for pleuropneumonia, 424
for right dorsal colitis, 142-143
neonatal metabolism of, 3
side effects of, 424
- Metronidazole for pleuropneumonia, 424
- MIC. *See* Minimum inhibitory
concentration (MIC)
- Michel's transport media, 364
- Miconazole (Monistat 7), 479t
for ocular emergencies, 463t
- Miconema deletrix*, 775
- Microangiopathic hemolysis, 345
- Microbial culture in tracheal aspirates,
406
- Microorganisms in tracheal aspirates,
405-406
- Micropolyspora faeni*, 793
- Microsporum gypseum*, 199
dermatophytosis, 191
- Middiaphyseal humeral fractures, shock
wave therapy for, 565
- Middle gluteal, pain in, 495
- Middle meatus, examination of, 368
- Midmetacarpus, deep digital flexor
tenotomy in, 527
- Midpalmar pastern, T2-weighted image
of, 510f
- Midpastern, deep digital flexor tenotomy
in, 527
- Migration action potential complex
(MAPC), 127
- Milk sickness, 783
- Milk-face, 634
- Milkweed, 783
- Mineral oil
for cantharidin toxicosis, 785-786
for dehydration, 119
for esophageal obstruction, 93
for ionophore toxicity, 745
for large colon impaction, 133
for rectal prolapse, 325
- Minerals
for exertional rhabdomyolysis, 730
in feed, 721t
in parenteral nutrition, 113
- Miniature Horses
atropine for, 557
mares, vaginal adhesions in, 327
- Miniature Horses—cont'd
packed cell volume of, 337
prekallikrein deficiency in, 353
- Minimum inhibitory concentration
(MIC), 9, 850
- Minnows, 194
- 4-minopyridine, avoidance of, 745
- Minoxidil for alopecia areata, 215-216
- Minute ventilation in foals, 687
- Miosis, 462, 478
- Misoprostol
for neonatal gastric ulcers, 5
for right dorsal colitis, 142
- Mites, 187-190, 188t
control of, 190
pruritus associated with, 189-190
- Mitotic drugs for glaucoma, 487
- Mitral insufficiency, 615
- Mitral regurgitation, 615-617
atrial fibrillation with, 615
M (motion) mode echocardiography,
616f
murmurs, 615
- Mitral valve
auscultation of, 575
color-flow Doppler, 616
parasternal long-axis view, 616
pulsed-wave Doppler, 616
- MMAD. *See* Mass median aerodynamic
diameter (MMAD)
- MMPs. *See* Matrix metalloproteinases
(MMPs)
- Modified sepsis score, 659t
- Modified Stoll's technique, 162
- Modified Viborg surgical approach,
387
- Modified Whitehouse surgical approach,
387
- Molar cutters, 84
- Molar table angle, 82-83, 83f
- Molasses
for hepatic failure, 172
oral administration of, 7
- Mold allergies, 181, 793-794
- Mold-induced diseases, 792-793
- Molds, 779, 792-794, 793t
- Moldy corn disease associated with signs
of forebrain disease, 765-766
- Moldy feed, 792
- Molecular markers, 513
- Molecular mimicry, 346
- Monensin intoxication, 620
- Monistat 7. *See* Miconazole (Monistat 7)
- Monoclonal antibodies for endotoxemia,
107
- Monoclonal protein, 361
- Monocular depth perception, 455
- Monosporium*, 792
- Moon blindness, 468-473
- Morbillivirus (Hanta virus) causing
interstitial pneumonia, 426
- Morgan horses
equine degenerative
myeloencephalopathy in, 748
with cecal impaction, 138
- Morphine, 18
for colic, 117
in critical care, 20
- Mosquitoes, 186, 194
breeding sites
elimination of, 770
larval habitat control, 194
- Moth-eaten alopecia, 187
- Motility, 101
- Motion, sensitivity to, 455

- Motor unit disorders
 ancillary diagnostic tests in, 744
 differentiation of, 743t
 muscle groups affected, 742
 Mountain thermopsis, 782
 Mounting, difficulties with, 318
 Moxidectin
 cyathostomiasis resistance to, 162-163
 for brainstem disease, 777
 for intestinal tapeworm, 159
 for skin parasites, 196
 Moxifloxacin, 6
 MRI. *See* Magnetic resonance imaging (MRI)
 MSM. *See* Methylsulfonylmethane (MSM)
 Mucoid ocular discharge, 490
 Mucokinetic agents for heaves, 420
 Mucolytics
 for foal pneumonia, 672
 for heaves, 420
 Mucopurulent odor discharge, 490-491
Mucor, 792
 Mucosal flap formation of, 382
 Mucosal injury, 410
 Mucous membrane, color of, 573
 Mucus
 in inflammatory airway disease, 413
 in tracheal aspirates, interpretation of, 403-404
 Mud fever, 201-203
 Mud rash, 201-203
 Multicentric lymphoma, 359
 Multiform ventricular arrhythmias, 617-619
 Multiple myeloma, 361
 in Quarter horses, 362
 Multisystemic eosinophilic epitheliotropic disease (MEED), 147
 Mupirocin ointment (Bactoderm) for equine pastern dermatitis, 202
 Murmurs, 575-576
 associated with structural disease, 595-596
 continuous, echocardiogram indications for, 614b
 definition of, 575-576
 duration of, 576
 in foals, 687
 with thrombophlebitis, 626
 Murray Valley encephalitis, 766
Musca autumnalis, 194
Musca domestica, 51, 194
 Muscle relaxants, 19
 Muscles
 atrophy of, 493
 biopsy of and chronic exertional rhabdomyolysis, 728-729
 chronic pain of, 569
 dysfunction of and inflammatory upper airway disease, 398-399
 enzymes of and chronic exertional rhabdomyolysis, 728
 palpation of, 495
 soreness of, manual therapy of, 567
 Muscular hypertrophy, 128
 Musculocutaneous nerve, damage to, 735
 Musculoskeletal diseases, 721-722
 Musculoskeletal disorders. *See also* Orthopedic disease
 complementary therapy for, 567-571
 manual therapy of, 567-568
 Musical murmurs, 613
 Myalgia in motor unit disorders, 744
 Myasthenia, 740-745
 clinical signs of, 741-742
 differential diagnosis of, 742-744
 etiology of, 740-741
 pathogenesis of, 740-741
 prognosis of, 745
 treatment of, 745
 Myasthenia gravis
 acquired, diagnosis of, 744
 differentiation of, 743t
Mycobacterium bovis, cell wall extract of, 446-447
Mycobacterium causing thromboembolic events, 620
Mycobacterium paratuberculosis, 146
Mycoplasma causing interstitial pneumonia, 426
 Mycosis fungoides, 209, 360
 Mycotoxins, 779, 792-794, 793t
 Mydriasis, 453
 Mydriatic/cycloplegics
 for corneal lacerations, 465
 for corneal ulcers, 466
 for eyelid lacerations, 465
 for fungal keratitis, 478
 for ocular emergencies, 464t
 for stromal abscess, 466
 for uveal injuries, 466
 Myelitis with penile paralysis, 304
 Myelodysplastic syndromes, 362
 Myeloencephalitis, 754
 Myeloid leukemia, 362
 Myeloid to erythroid ratio (M:E), 339
 Myelophthisis, 349
 Myeloproliferative disorders, 359-362
 Myelophthisis, anemia due to, 343
 Myiasis, 194
 Myocardial disease, 620-624
 clinical signs of, 620
 laboratory findings in, 620-621
 prognosis of, 621
 treatment of, 621
 Myocardial fibrosis, 611
 Myocarditis, 596, 611
 Myodegeneration, 744
 Myofascial pain syndromes, 569
 Myoglobin-induced nephropathy, 842
 Myoglobinuria, 744
 N
 NADPH. *See* Nicotinamide adenine dinucleotide phosphate (NADPH)
 NAHMS. *See* National Animal Health Monitoring System (NAHMS)
 Naloxone hydrochloride (Narcan)
 for acute blood loss, 341
 in critical care, 21-22
 Nandrolone decanoate (Deca-Durabolin), 343
 NaPPS. *See* Sodium pentosan polysulfate (NaPPS)
 Naproxen (Equiprofen) for joint disease, 560
 Naquasone. *See* Trichlormethiazide-dexamethasone (Naquasone)
 Narcan. *See* Naloxone hydrochloride (Narcan)
 Narcolepsy, 771
 Nasal cavities
 examination of for laryngeal hemiplegia in non-racehorses, 384
 neoplasms of resembling progressive ethmoid hematoma, 375
 packing of for hemorrhage control, 376
 Nasal dilator strips for exercise-induced pulmonary hemorrhage, 432
 Nasal discharge, 401
 in sinus disease, 369
 Nasal edema, 391, 392
 Nasal insufflation, 428
 Nasal neoplasms, 340
 Nasal passage
 centesis of, 371-372
 computed tomography of, 371
 endoscopy of
 examination of, 368
 nuclear scintigraphy of, 371
 radiography of, 370-371
 Nasal passages
 endoscopic view of, 370f
 endoscopy of, 370
 radiographic view of, 370f
 Nasogastric intubation
 for duodenitis-proximal jejunitis, 122
 for esophageal obstruction, 91
 prolonged, complications of, 122-123
 relieving gastric tympany, 115
 Nasolacrimal drainage, integrity of, evaluation of, 465
 Nasolacrimal duct
 composition of, 489
 congenital obstruction of, 490
 infection of resembling progressive ethmoid hematoma, 375
 retrograde placement of lavage tubing, 459
 Nasolacrimal patency, 451
 Nasopharynx, examination of for laryngeal hemiplegia in non-racehorses, 384
 Nasotracheal intubation, 691f
 Natamycin, 479t
 for folliculitis, 200
 for ocular emergencies, 463t
 National Animal Health Monitoring System (NAHMS), 56
 Natural colloid therapy, 355-356
 Natural reduction, 246
 Navel dip solution, 323
 Navicular bone, 532
 proton density image of, 512f
 Navicular bursa, 532
 Navicular degeneration, magnetic resonance imaging of, 509
 Navicular disease, definition of, 498
 Navicular ligaments, 532
 Navicular syndrome, 500
 aspirin for, 559
 extracorporeal shock wave therapy for, 566
 Naxcel. *See* Ceftiofur (Naxcel)
 Nd/YAG laser. *See* Neodymium/yttrium-aluminum-garnet (Nd/YAG) laser
 Nebulization for foal pneumonia, 672
 Nebulizers, 437
 Nebulizing formula for foal pneumonia, 673b
 NEC. *See* Necrotizing enterocolitis (NEC)
 Neck, palpation of, 495
 Necrotic lung, 421
 Necrotizing enterocolitis (NEC), 644
 Nedocromil sodium for recurrent airway obstruction, 443
 Nedocromil sodium (Tilade) for heaves, 420
 Needle electromyography, 744
 Negative-pressure pulmonary edema, 393
 causing postanesthetic upper respiratory tract obstruction, 392

- Negligence regarding rectal tears, 152
 Neoantigens, 346
 Neodymium/yttrium-aluminum-garnet (Nd/YAG) laser, 394
 for distal tarsal joint arthrodesis, 541
 for glaucoma, 487
 for progressive ethmoid hematoma, 377
 Neomycin
 for foal pneumonia, 671
 for hepatic failure, 172
 for pyrrolizidine alkaloid poisoning, 790
 Neomycin-polymyxin-gramidicin, 475
 Neonatal drug absorption, 1
 Neonatal endotoxemia, 4
 Neonatal foals. *See* Newborn foals
 Neonatal gastric ulcers, 5
 Neonatal intensive care units (NICUs), 631
 Neonatal isoerythrolysis, 345, 636-640
 clinical signs of, 636
 diagnosis of, 636-637
 laboratories providing diagnostic services for, 639t
 prevention of, 637-638
 tests for, 638f
 treatment of, 638-640
 Neonatal maladjustment syndrome (NMS), 644, 655. *See* Hypoxic ischemic encephalopathy
 Neonatal pharmacology, 1-3
 altered absorption, 1
 dosage, 1, 2t
 elimination, 3
 metabolism, 3
 volume of distribution, 3
 Neonatal respiratory distress syndrome (RDS), 643
 Neonatal seizures, 5
 Neonatal sepsis, 3-4
 Neonatal septicemia, 656-662
 antimicrobials for, 661t
 early intervention strategy for, 658
 laboratory investigation of, 658
 risk factor recognition in, 656
 sepsis recognition in, 656-658
 Neonatal therapeutics, 3-5
 Neonates
 Clostridium difficile infection in, 167
 evaluation of, 323-324
 immunity in, 692
 Neoplastic effusions caused by lymphosarcoma, 423-424
Neorickettsia actinomycete, 298
Neorickettsia risticii, 58, 74
 causing weanling diarrhea, 165
 vaccine, 252
Neospora caninum, 69
Neospora hughesi, 69
 Neostigmine
 avoidance of, 745
 for cecal impaction, 140
 for ileus, 110
Neotrombicula, 188
Neotyphodium coenophialum, 796
 Nephrolithiasis, 832-833
 Nephrosplenic entrapment of large colon, 149
 Nephrosplenic space, large colon displacement into, 149
 Nephrotoxicity, hematuria, 854
Nerium oleander, 783
 Nerve blocks, 500
 Nerve conduction velocity, measurement of, 739
 Neuraminidase, 42
 Neuritis
 of cauda equina, 756
 treatment of, 476
 Neurofibroma with cauda equina, 758
 Neurogenic incontinence, 824-825
 Neurologic disease, ocular signs secondary to, 476
 Neurologic examination of cauda equina damage, 758
 Neuromas of peripheral nerves, 740
 Neuromuscular junction disorders, disorders causing, 741t
 Neuroophthalmic examination, 451-452
 Neuropeptide as neurotransmitter, 109
 Neutropenia caused by endotoxemia, 108
 Neutrophilic leukocytosis, 61
 Neutrophils, 228, 228f
 in bronchoalveolar lavage, 409, 411f
 in ischemia-reperfusion injury, 136
 in tracheal aspirates, 405
 New Jersey vesicular stomatitis virus (VSV-New Jersey), 51
 New Zealand, stringhalt in, 761
 Newborn foals, 633-634
 cardiopulmonary resuscitation of, 650-655
 care of foals after, 654-655
 cessation of, 654
 equipment for, 650-651
 monitoring of, 654
 ordered plan for, 651-654
 normal blood volume of, 640
 sick, 631-635
 NFDSM-G extender. *See* Nonfat dry skim milk-glucose (NFDSM-G) extender
 Niacin in parenteral nutrition, 113
 Nicotinamide adenine dinucleotide phosphate (NAPDH), 135
 Nictitating membrane, 452
 seromucoid gland of, 488
 Nictitating membrane, laceration of, 465
 NICUs. *See* Neonatal intensive care units (NICUs)
Nidovirales, 36-38
 Nighttime foaling attendant, 323
 Nigropallidal encephalomalacia, 779, 780-781
 Nitric oxide
 as neurotransmitter, 109
 for exercise-induced pulmonary hemorrhage, 432
 Nitric oxide synthase (NOS) for exercise-induced pulmonary hemorrhage, 432
 Nitrofurazone
 for axial deviation of the aryepiglottic folds, 380
 for cutaneous habronemiasis, 196, 305
 Nitroglycerine, 77
 for exercise-induced pulmonary hemorrhage, 432
 Nizoral. *See* Ketoconazole (Nizoral)
 N-methyl-D-aspartate (NMDA) receptors, 645
 NMS. *See* Neonatal maladjustment syndrome (NMS)
Nocardioform actinomycete causing placentitis, 297, 298
 Nodular necrobiosis, 206-207
 Nolvavan for vesicular stomatitis, 53
 Noncollagenous protein assays, 518
 Nonfat dry skim milk-glucose (NFDSM-G) extender for semen motility assessment, 267
 Nonglandular mucosa, ulcers in, 95
 Nonlactating mares for embryo transfers, 278
 Nonneoplastic sterile nodules, 206-208
 Nonneurogenic incontinence, 824
 Nonparasitic mites, 189
 Non-racehorses, laryngeal hemiplegia in, 383-386
 Nonspecific lameness, manual therapy of, 567
 Nonsteroidal antiinflammatory drugs (NSAIDs), 11-14, 460
 adverse effects of, 12, 94-95
 authorized use of in racing, 32
 causing large colon impaction, 131
 causing oral ulceration, 90
 causing right dorsal colitis, 141
 for abdominal laparoscopy, 149
 for acquired pericardial disease, 623
 for cecal impaction, 139
 for cervical stenotic myelopathy, 748
 for colic, 115-116
 for duodenitis-proximal jejunitis, 123
 for endotoxemia, 107
 for endotoxin, 21
 for equine influenza, 43
 for equine recurrent uveitis, 470
 for equine viral arteritis, 37-38
 for esophageal obstruction, 93
 for foal pneumonia, 672
 for foals, 691
 for fungal keratitis, 478-479
 for ileal impaction, 128
 for jugular vein thrombophlebitis, 626
 for neonates, 5
 for penile trauma, 303
 for perinatal equine herpesvirus-1 infection, 41-42
 for peripheral nerve disease, 739
 for peritonitis, discontinuation of, 157
 for permanent tracheostomy in standing horses, 397
 for rectal prolapse, 325
 for salmonellosis, 59
 for spinal cord trauma, 749
 for strangles, 66
 for stromal abscess, 466
 for ulcerative keratomycosis, 466
 for uveal injuries, 466
 for vaginal lacerations, 327
 for vasculitis, 365
 for viral encephalitides, 770
 in critical care, 19-20
 in racing, 34
 neonatal volume of distribution, 3
 renal toxicity of, 12
 with right dorsal colitis, 142
 Nonsuppurative inflammatory hepatitis, chronic, treatment of, 172-173
 Nonsurgical embryo transfers, 283
 Norepinephrine, release of, 109
 Normal blood volume of neonatal foal, 640
 Normal cardiac development, 591-592
 Normal heart sounds, 575-576
 Normal maternal-foal behavior, 264
 Normal ovaries, 260
 Normal parturition, 319-320
 Normal sinus rhythm, 603f
 Normosol-R, 113, 119, 685
 for cardiopulmonary resuscitation of newborn foal, 653
 for postpartum hemorrhage, 329
 Northern raccoon (*Procyon lotor*), 69
 No-see-ums, 191

- NRC National Research Council's Nutrient Requirements of Horses, 704, 719
- NSAIDs. *See* Nonsteroidal antiinflammatory drugs (NSAIDs)
- Nuclear scintigraphy
after regional anesthesia, 500-501
in prepurchase examination, 501-502
in racehorses, 500
multiple problem screening, 501
of cauda equina damage, 758
of foot lameness in performance horse, 500
of nasal passage, 371
of urinary tract, 823
poor performance screening, 501
referral, 500-502
- Nurse mares, 265
- Nutraceuticals, 26-29
- Nutrient metabolism, 112
- Nutrition, abnormal, 705
- Nutritional deficiency causing inadequate erythropoiesis, 342-343
- Nutritional ergogenic aids, 28-29
- Nutritional management for chronic laminitis, 526
- Nutritional myodegeneration, 741
differentiation of, 743t
- Nutritional needs of breeding stallions, 252
- Nutritional support for *Clostridium difficile* infection, 168
- Nutritional therapy
field application of, 710
for acutely ill horse, 708
for colitis, 723-724
for exertional rhabdomyolysis, 727-728, 727-734
for gastrointestinal disease, 722-726
for postoperative colic surgery patients, 722-723
for rectal tears, 726
- Nymphomania, 262
- Nystagmus, secondary to neurologic disease, 476
- O**
- Oat hay, mineral content of, 721t
- Oats, mineral content of, 721t
- Obesity, 715-716, 812
insulin refractory state, 812-813
laminitis, 813-814
- Obesity-associated insulin refractory state, 814
- Oblique distal sesamoidian ligament, 499
- Observation during prepurchase examination, 495-496
- Obstetrical cases, 296
- Obstetrical chains for dystocia, 320
- Obstetrics, 319-322
- Obstructing enteroliths, 149
- OCD. *See* Osteochondrosis dissecans (OCD)
- Ocular adnexa, examination of, 452
- Ocular discharge
abnormal, 488-492
diagnosis of, 491
characterizing, 489-490
- Ocular emergency
definition of, 461
drugs for, 463t
- Ocular infection, barrier to, 477
- Ocular lavage system, 458-459
- Ocular pain, acute, 462
- Ocular therapy, 457-461
- Ocular trauma, emergency treatment of, 461-467
- Oculocephalic reflexes, 451
- Oculopupillary reflex, 474
- Oils, 698
recommendations for, 703-704
- Ointments, 458
- Older mares, embryo transfers in, 277
- Oleander, 783
- Oliguria, 841
- Omeprazole
for esophageal obstruction, 93
for gastric ulcers, 98
for neonatal gastric ulcers, 5
for perinatal asphyxia syndrome, 648t
for ulcers, 22
- Once-daily aminoglycoside dosing regimen, 850-853
- Onchocerca*, 468, 474
- Onchocerca cervicalis*, 184, 193
- One-way flutter valve, 423
- Onions, 344
- Oocytes
collection of, 286
donors of, synchronization of, 285-286
evaluation and culture of, 286
recipients of
insemination of, 287
synchronization of, 285-286
transfer of, 285-287, 286-287
future of, 287
- Opacification, 466-467
- Open chest drainage, 423
- Open pneumothorax, 434
- Open-ended artificial vagina, 255
- Ophthalmic examination, 462
- Ophthalmic examination, horse restraint for, 451
- Ophthalmic instrumentation, 450-451
- Ophthalmologic drops for skin parasites, 196
- Opioids
for colic, 115-116, 117
in critical care, 20
- Optic nerve
atrophy of, 467
damage of, by blunt head trauma, 467
emergencies involving, 467
ischemia of, 467
- Optic nerves of large eyes, 486
- Optic neuritis, secondary to neurologic disease, 476
- Optics, 454-459
- Optimal feeding, 698
- Oral administration, 7
- Oral corticosteroids, 460
- Oral electrolyte therapy, 119t
- Oral examination, 706
- Oral fluid therapy for dehydration, 117-118
- Oral laxatives
for colic, 119-120
for rectal prolapse, 325
- Oral ulceration
causes of, 89-90
differential diagnosis of, 88-90
regulations regarding, 90
viral causes of, 88-89
- Orbifloxacin, 10
- Orbit, 462-464
- Orbital rim, 462-464
- Orchardgrass, mineral content of, 721t
- Orchitis, 308
- Organic acids, 95
- Organochlorines for mite control, 190
- Organophosphate insecticides, 786
- Organophosphates
for cutaneous habronemiasis, 305
for equine pastern dermatitis, 203
for mite control, 190
- Ornithine carbamoyltransferase, 169
- Orphan foals
nurse mares for, 265
with diarrhea, 677
- Orthopedic disease
magnetic resonance imaging of, 509-510
postoperative management of, 544-546
preoperative pain management, 544
- Orthopedic felt, 549, 550
- Orthopedic stockinette, 549
- Oryzanol, 29
- Oscillometry, 415
- Osmotic diarrhea, 849
- Osmotic pressure for semen extenders, 267
- Osseous injuries, magnetic resonance imaging of, 509
- Osseous sequestra, 537-540
metacarpal region in, radiography of, 538f-539f
prevention of, 539-540
treatment of, 538-539
- Osteoarthritis, 14-16
complementary therapy for, 570
extracorporeal shock wave therapy for, 565
intraarticular hyaluronan for, 555-556
pathogenesis of, 558
sulfated glycosaminoglycans in, 514-515
- Osteocalcin, 518
- Osteochondrosis dissecans (OCD)
in tibial tarsal joint, 499
of trochlea, 499
- Osteomyelitis, 61, 527
in neonates, 657-658
of distal phalanx, antibiotics for, 526
- Osteostitis, 539
- Otobius megnini*, 189
- Otobius* nymphs, 190
- Outlet ventricular septal defects (VSD), 596
- Ovarian artery, 327
- Ovarian senescence, 261
- Ovariectomy for granulosa cell tumors, 262
- Ovaries, 260
anabolic steroid effect on, 261
cystadenomas of, 262
dysgerminomas of, 262
enlarged, 261-263
evaluation of, 260-261
loss of shape with granulosa cell tumors, 262
shape of, 260
size of in after foaling mare, 249
teratoma of, 262, 263f
ultrasound of in recipient mares, 278
- Overbite, 86
- Overfeeding, 715
causing large colon impaction, 131
- Overheating in inflammatory airway disease, 413
- Overhydration, 420
- Overweight mares causing angular limb deformities, 663
- Ovulation
induction of, 240-242, 273
interval to, 272-273
monitoring of, 245

- Ovulation—cont'd
 prediction of, 242-245
 timing of, 249
 Ovulation fossa, 260
 Ovulation induction, insemination
 protocols for, 241b
 Ovulation-inducing agents, 273
 Ovuplant. *See* Deslorelin acetate
 (Ovuplant)
 Ovuplant for recipient mares, 279
 Owner education
 for penile hygiene, 836
 for recurrent airway obstruction, 441
 Owner noncompliance with laminitis
 treatment, 528
 Oxidative erythrocyte damage, 344-345
 Oxidizing agents, 25, 344
 Oxygen
 for foal pneumonia, 672
 for hypoxia, 345
 for negative-pressure pulmonary
 edema, 393
 Oxygen tension, assessment of, 137
 Oxygen toxicity causing interstitial
 pneumonia, 426
 Oxyglobin, 357, 640
 Oxyphenbutazone, 13-14
 Oxytetracycline
 for equine monocytic Ehrlichiosis, 77
 for neonates, 4
 for vasculitis, 365
 Oxytocin
 during artificial insemination, 278
 enhancing uterine clearance, 231
 for abdominal wall hernias, 310
 for esophageal obstruction, 93
 for parturition induction, 316
 for persistent mating-induced
 endometritis, 236
 for retained fetal membranes, 331, 332
Oxytropis, 767
- P**
 P wave, 576, 602
 Pacing and trotting, 429
 Packed cell volume (PCV), 355
 in foals, 688
 in peritonitis, 154
 with anemia, 337
 PAE. *See* Postantibiotic effect (PAE)
Paecilomyces, 792
 Painful joints, cutaneous points relating
 to, 495
 Paint, squamous cell carcinoma in, 480
 Palmar lesions, computed tomography
 of, 506
 Palmar subchondral lysis, 498
 Palominos, alopecia areata in, 215
 Palpation
 during prepurchase examination, 495-
 496
 horse's reaction to, 495
 in prepurchase examination, 493
 Palpation per rectum
 of after foaling mare, 249
 of broad ligaments, 313f
 of postpartum hemorrhage, 328
 of recipient mares, 278
 of uterine torsion, 312
 Palpebral reflexes, 451
 PAM. *See* Pulmonary alveolar
 macrophages (PAM)
 Panoramic view, 455
 Pantothenic acid in parenteral nutrition,
 113
 Pantyhose sling, 303
 Paper trace echocardiographies, 602
 Papillomas, congenital, 212
 Papillomatosis, 212
 Papillomavirus-induced oncogenic
 transformation, 204
Papoxvirus ovis, 447
 Paracostal approach for cesarean section,
 322
 Paracrine factors, 257
 Paracrine/autocrine system, 257
 Parainfluenza type 3, 469
 Paralytic ileus in postoperative colic, 111
 Paramagnetic contrast with radiographic
 contrast, 509-510
 Paramembranous defects, 596
 Paranasal sinus, 369
 Paranasal sinuses
 neoplasms of resembling progressive
 ethmoid hematoma, 375
 packing of for hemorrhage control, 376
 Paraneoplastic syndrome, 360
 mucocutaneous form of, 89
 Paraphimosis, 304f
 Parapneumonic effusion, athletic horses
 with, 408
 Paraprotein, 361
 Paraquat, 675
 Pararectal cystotomy, 834
Parascaris equorum, 164
 causing interstitial pneumonia, 426
 Parasites, 197
 in foal pneumonia, 666
 in interstitial pneumonia, 425
 Parasitic encephalitis, 775
 Parasternal long-axis view, mitral valve,
 616
 Parasympathetic nervous system effect
 on gastrointestinal motility, 109
 Parelli, Pat, 570
 Parenteral administration, 7
 Parenteral corticosteroids for interstitial
 pneumonia, 428
 Parenteral nutrition
 administering, 113-114
 components of, 112-113
 cost of, 113
 for colic, 111-115
 for failure of passive transfer, 694-695
 for myasthenia, 745
 for neonatal septicemia, 662
 for perinatal asphyxia syndrome, 649
 formulas for, 114t
 preparation of, 113
 with compromised gastrointestinal
 function, 717
 Paresis, evaluation of, 746
 Parity
 and endometrial cysts, 231
 and inability to clear uterus, 234
 Paromomycin for foal diarrhea, 678
 Parotid lymph nodes (PLN), 64
 Parovarian (fimbrial) cysts, 261
 Paroxysmal arrhythmias, recording of,
 577
 Paroxysmal atrial fibrillation, 606
 Parrot-mouthed horses, 86, 86f
 Pars intermedia, 812, 813
 Partial arytenoidectomy, 382
 Partial phallectomy, 836
 Parturition
 induction of, 315-317
 criteria for, 315-316
 method of, 316-317
 placental evaluation after, 298
 Parturition—cont'd
 signs of problems during, 633
 stages of, 319-320
 Paso Fino, 486
 Passive immunization for *Rhodococcus*
equi infections, 63
 Passive transfer of immunoglobulins,
 assessment of, 693-694
 Pastern
 proton density image of, 510f
 radiography of, 498
 temperature of, 503
 Pastern leukocytoclastic dermatitis, 175
 Pastern leukocytoclastic vasculitis, 175
 Pastern leukocytoclastic vasculopathy,
 175
Pasteurella, 6, 851
 in foal pneumonia, 666
 in foals, 3
 in jugular vein thrombophlebitis, 626
 Pasture harrowing for resistant
 cyathostomiasis, 164
 Pastures, 701
 feed-related toxicoses, 779
 management of, 798
 Patella, upward fixation of, 536-539
 Patent ductus arteriosus, 601, 646
 Patent urachus, 827
 Pathologic bradydysrhythmias, 604-610
 PCR. *See* Polymerase chain reaction (PCR)
 PCV. *See* Packed cell volume (PCV)
 PD. *See* Proton density (PD)
 PDE. *See* Phosphodiesterase (PDE)
 Peanut kernels, 420
 Peat moss, 420
 Pectins, 698
 Pedal osteitis, 498
Pediculoides ventricosus, 189
Pediococcus, 27
Pediococcus acidilactici, 27
 PEEP valve. *See* Positive end-expiratory
 pressure (PEEP) valve
 Pelleted feed enteral formulation, 709t
 Pelleted hay, 420
 Pemphigus foliaceus, 178, 197, 217-218
 histopathology of, 179
 Pendulant kidney, 828
 Penetrating keratoplasty for corneal
 ulcers, 466
 Penetrating ocular trauma, 467
 Penetrating wounds in pneumothorax,
 434
 Penicillin, 6
 for cystitis, 838
 for jugular vein thrombophlebitis, 626
 for neonatal septicemia, 3
 for pleuropneumonia, 424
 for proliferative enteropathy, 165
 for rectal tears, 152
 for strangles, 66
 Penicillin G
 for foal pneumonia, 671
 for neonatal septicemia, 661t
 injection of, 248
 Penicillin-aminoglycoside for retained
 fetal membranes, 332
Penicillium, 477, 792
 Penis
 aerobic bacterial cultures of, 269
 amputation of, 304, 836
 granulomas of, 305
 injured, support of, 304f
 neoplasms of, 305
 paralysis of, 304
 relaxation of, 755

- Penis—cont'd
 resection of, 836
 surgical retraction of, 304
 trauma of in breeding stallion, 303-304
- Penis detumescens, 318
- Penlight, 450
- Pentology of Fallot, 599
- Pentobarbital
 dosage of, 769t
 for perinatal asphyxia syndrome, 648t
- Pentosan polysulfate (PPS), 561
- Pentoxifylline (Trental)
 for duodenitis-proximal jejunitis, 123
 for EHV-1 myeloencephalitis, 752
 for endotoxemia, 107
 for endotoxin, 21
 for equine pastern dermatitis, 203
 for exercise-induced pulmonary hemorrhage, 433
 for fetal compromise, 632
 for heaves, 419
 for placental hydrops, 302
 for placentitis, 300
 for salmonellosis, 59
- Pepsin, 95
- Peptostreptococcus*, 6
- Percussion in sinus disease, 369
- Percutaneous abdominal lavage for
 peritonitis without intestinal
 rupture, 156-157
- Perforating gastric ulcer in foals, 96
- Performance and energy sources, 702-703
- Performance horses
 cardiovascular function of
 evaluation of, 585-591
 history of, 586
 physical examination of, 586
 standardized exercise testing, 586-587
 drug testing in, 32-35
 foot lameness in, nuclear scintigraphy
 of, 500
 inflammatory airway disease in, 412-
 417
 lameness in, treatment of, 559
 multiple problem screening in, 501
- Perfusion in foals with colic, 681
- Pergolide, 810
 for Cushing's syndrome, 526
- Periarticular ligamentous laxity,
 treatment of, 664
- Pericardial disease, acquired, 622-623
- Pericardial effusion, 622
- Pericardial friction rubs, 622
- Pericardial stripping, 623
- Pericardiectomy, 623
- Pericardiocentesis, 623
- Pericarditis, 596, 622
- Perilla ketone causing interstitial
 pneumonia, 426
- Perimembranous defects, 596
- Perinatal asphyxia syndrome
 central nervous system disease,
 differential diagnosis of, 646
 clinical signs of, 645-646
 in foals, 644-649
 laboratory findings in, 646
 periparturient events, 645
 treatment of, 647-648
- Perinatal equine herpesvirus-1 infection,
 41-42
- Perinatal period and premature foals, 642
- Perineal area, cleansing of for
 endometrial biopsy, 233
- Perineal lacerations, 333-334
 third-degree, 334f
- Periodic ophthalmia, 468-473
- Perioperative fatality rate of foals, 687t
- Periorbital cysts, computed tomography
 of, 507
- Periorbital fractures, 462-464
- Peripartum mares
 normal procedures for, 323
 peritoneal fluid in, 294-297
 peritoneal fluid sample from, 295
- Periparturient asphyxia
 clinicopathologic conditions associated
 with, 647t
 drugs for, 648t
- Peripheral aneurysm, 629
- Peripheral cushingoid syndrome, 717,
 812-815
 clinical signs of, 814
 diagnosis of, 814
 prevention of, 814-815
 treatment of, 814-815
- Peripheral edema in cardiovascular
 examination, 573
- Peripheral ganglionopathy of Fell ponies,
 696-697
- Peripheral lung abscesses, 421
- Peripheral nerve disease, 735-740
 diagnosis of, 735-738
 differential diagnosis of, 739-740
 neurodiagnostic evaluation of, 739
 treatment of, 739-740
- Peripheral quantitative CT scanners
 (pQCT), 505, 505f
- Peritoneal effusion, 149
- Peritoneal fluid, 857
 analysis of, 295
 in foals, 684-685
 cytology of, 155
 in peripartum mares, 294-297
 microbial culture of, 155
 obstetrical complications effect on,
 295-297
- Peritonitis, 153-158, 627
 characterization of, 148-149
 clinical signs of, 153-154
 diagnosis of, 154-155
 monitoring clinical response to
 treatment of, 157
 treatment of, 155-158
 without intestinal rupture, treatment
 of, 155-156
- Perivascular dermatitis with eosinophilia,
 181
- Permanent tracheostomy
 in standing horses, 396-398
 aftercare of, 397
 prognosis of, 397-398
 surgical technique for, 397
 indications for, 396-397
- Permethrin, 185, 193
 for equine pastern dermatitis, 203
- Peromyscus leucopus*. See White-footed
 mouse (*Peromyscus leucopus*)
- Perphenazine for ergopeptide alkaloid
 toxicosis, 797, 798
- Perrilla mint ketone, 675
- Persistent mating-induced endometritis,
 234-237
 clinical signs of, 235
 diagnosis of, 235-236
 history of, 235
 pathogenesis of, 235f
 pathophysiology of, 234-235
 treatment of, 236-237
- Persistent penile erection, 304f
- Persistent postbreeding endometritis, 243
- Persistent truncus arteriosus, 600
- Pesticides for fly control, 192b
- Petroleum jelly, 191
- PGE2. See Prostaglandin E2 (PGE2)
- PH for semen extenders, 267
- Phaenicia*, 194
- Phalangeal cast, application of, 550f
- Phallectomy, 304
- Phallopepy, 304
- Phantom covers, 303
- Pharmaceutical compounding, 29-31
 benefits of, 30
 definitions of, 29
 practical considerations of, 31
 professional guidance for, 31
 regulation of, 30-31
 risk of, 30
- Pharyngeal lymphoid hyperplasia, 399
- Pharynx
 cysts of, laser surgery of, 395
 neoplasms of resembling progressive
 ethmoid hematoma, 375
 stiffness of, 367-368
- Pheasant eye, 783
- Phenobarbital
 dosage of, 769t
 for perinatal asphyxia syndrome, 647,
 648t
- Phenolics, 25
- Phenothiazine, 17-18, 344
- Phenothiazine-based tranquilizers, 265
- Phenoxybenzamine
 for EHV-1 myelitis, 754
 for EHV-1 myeloencephalitis, 752
 for incontinence, 825
- Phenylbutazone, 13-14
 causing anemia, 343
 for arytoid chondrosis, 382
 for axial deviation of the aryepiglottic
 folds, 380
 for *berteroia incana* toxicosis, 788
 for distal tarsal joint arthrodesis, 540-
 541
 for endotoxemia, 107
 for equine recurrent uveitis, 470,
 471t
 for foal pneumonia, 672
 for foals, 691
 for glaucoma, 487
 for joint disease, 558-559
 for mounting and thrusting difficulties,
 318
 for neonates, 4, 5
 for ocular emergencies, 463t, 464t
 for perineal lacerations, 333
 for peripheral nerve disease, 739
 for placentitis, 300
 for retained fetal membranes, 332
 for strangles, 66, 67
 for thermal burns, 222
 for upper respiratory tract postoperative
 management, 395
 for vasculitis, 365
 half-life of, 558
 in critical care, 20
 in racing, 34
- Phenylephrine for dysrhythmias, 604t
- Phenylethyl alcohol, 229
- Phenylpyrazole (fipronil) for mite
 control, 190
- Phenytoin
 for dysrhythmias, 604t
 for stringhalt, 761
 for ventricular ectopic beats, 611
- Philips Tomoscan, 505

- Phlebotomy
for exercise-induced pulmonary hemorrhage, 433
for polycythemia, 358
Phormia regina, 194
Phosphodiesterase inhibitor reducing tumor necrosis factor- α , 124
Phosphodiesterase (PDE) for heaves, 419
Phospholine iodide for skin parasites, 196
Phosphorus in feed, 721t
Photoc gate, 240
Photoactivated vasculitis, 364
Photoallergy, 174
contact agents associated with, 175b
Photochemistry, 174
Photodermatitis, 174, 789
Photometric instrument for sperm concentration determination, 267
Photoperiod manipulation, 237-240
Photophobia, 478
Photoreceptors, topographic distribution of, 456
Photosensitivity, 174-176
clinical signs of, 176
congenital etiology for, 175
diagnosis of, 176
etiology of, 174-175
history of, 175-176
therapy of, 176
Phototoxicity, 174
Phoxim for mite control, 190
Phthisis bulbi, 466
Phycomyces, 792
Phylloerythrin, 174
elevated levels not associated with alkaloids, 175b
measurement of, 176
Physical examination
for laryngeal hemiplegia in non-racehorses, 384
of angular limb deformities, 663-664
Physical maturity of premature foals, 642
Physical therapy, 569
Physical trauma affecting spermatozoa, 266
Physiologic dysrhythmias, 603-604, 605f
Physiotherapy for myasthenia, 745
Piezoelectric shock wave generator, 563f
Pigmenturia-associated with systemic disease, 856
Pigmy rattlesnakes (*Sistrurus* sp.) causing intravascular hemolysis, 345
Pilocarpine (Piloptic) for glaucoma, 487
Piloptic. *See* Pilocarpine (Piloptic)
Pin firing, iatrogenic burns caused by, 222
Pinto, squamous cell carcinoma in, 480
Pipette for artificial insemination, 283
Pirbuterol for heaves, 419
Piroplasmosis, 347-348
Pituitary pars intermedia dysfunction (PPID), 807-811
clinical signs of, 807-808
diagnosis of, 808-809
prognosis of, 811
treatment of, 810-811
Placenta
components of, 297
endocrine monitoring of, 299-300
evaluation of after abortion, 298
infection of causing dystocia, 320
thickness of during late gestation, 299f
ultrasonographic evaluation of, 298-299
Placental fluids, appearance of, 632
Placental hydrops, 301-302
Placental insufficiency, 297
Placentitis, 297-300, 632
causing angular limb deformities, 663
causing retained fetal membranes, 330
clinical signs of, 298-300
diagnosis of, 298-300
etiology of, 297-298
prevention of, 300
signs of, 632
treatment of, 300
with neonatal septicemia, 656
Plamalyte for postpartum hemorrhage, 329
Plant myotoxins, 782
Plant sterols, 29
Plant toxins causing angular limb deformities, 663
Plantar lesions, computed tomography of, 506
Plant-induced equine myotoxicoses, 779
Plant-induced necrosis, 782-784
Plasma
for acute blood loss, 341
for *Clostridium difficile* infection, 168
for dehydration, 119
for disseminated intravascular coagulation, 354
for failure of passive transfer, 695
for hypoproteinemia, 143
for postpartum hemorrhage, 329
for thermal burns, 222
for thrombocytopenia, 350
source of, 356-357
Plasma adrenocorticotropin
concentration for pituitary pars intermedia dysfunction, 809-810
Plasma cell myeloma, 361-362
Plasma cells, 228
Plasma cortisol with pituitary pars intermedia dysfunction, 809
Plasma globulins in neonates, 3
Plasma protein in neonates, 3
Plasma selenium and chronic exertional rhabdomyolysis, 729
Plasma transfusion, 356-357
adverse effects of, 695
Plasmalyte, 113, 685
Plasmalyte A, 119
Plasmin, 353
Platelets, 349
Plates for valgus and varus deviations, 665
Pleural drainage in pleuropneumonia, 423
Pleural effusion, drainage of, 423
Pleural fluid, chest tube drainage of in pleuropneumonia, 423f
Pleural lavage in pleuropneumonia, 423
Pleuropneumonia, 105, 421-424
chest tube drainage of pleural fluid in, 423f
differentiation from neoplasia, 423-424
free gas echoes, sonographic appearance of, 422f
management of, 424
pleural drainage in, 423
pleural lavage in, 423
thoracic ultrasonography of, 421-423
Pleuroscopy, 423
PLN. *See* Parotid lymph nodes (PLN)
PLR. *See* Pupillary light reflex (PLR)
Plugged ampullae, 256
PMI. *See* Point of maximal intensity (PMI)
PMNs. *See* Polymorphonuclear leukocytes (PMNs)
Pneumatic splints for periarticular ligamentous laxity, 664
Pneumatic surgical drill, 539
Pneumatosis intestinalis, 646
Pneumocystis carinii
causing interstitial pneumonia, 426
in foal pneumonia, 666, 670
trophozoites in, 428
with acute respiratory distress syndrome, 674
Pneumocystis carinii pneumonia, 429
Pneumonia, 105, 790
differentiation from thoracic trauma, 433
in neonates, therapy of, 661
Pneumothorax, 434-435
detection of, 421-422
sonography of, 422f
Pneumotoxins, 675
POI. *See* Postoperative ileus (POI)
Point of maximal intensity (PMI), 576
Poliomyelomalacia, clinical signs of, 802
Polycystic kidneys, 827
Polycythemia, 358
Polydipsia, 830-831, 846
differential diagnosis of, 828-830
etiology of, flow chart of, 830f
Polyionic crystalloid for postpartum hemorrhage, 329
Polymerase chain reaction (PCR), 46
for equine monocytic Ehrlichiosis, 76
for interstitial pneumonia, 425
for *Rhodococcus equi* infections, 61
for semen testing, 253
Rhodococcus equi, 667-668
Polymorphonuclear leukocytes (PMNs), 272
Polymyxin B
for duodenitis-proximal jejunitis, 123
for endotoxemia, 106-107, 108
for endotoxin, 21
for ocular emergencies, 463t
for salmonellosis, 59
Polyneuritis equi, 735, 739, 756, 775
Polysaccharide storage myopathy (PSSM), 727, 728
potential rations for, 732t
recommended diets for, 731-733
Polysulfated glycosaminoglycans (PSGAGs), 14, 16
for joint disease, 560-561
Polysynovitis, 60-61
Polyuria, 831, 846
differential diagnosis of, 828-830
iatrogenic causes of, 831
Polyuria, etiology of, flow chart of, 830f
POMC. *See* Proopiomelanocortin (POMC)
Ponazuril
for EPM, 770
for lower motor neuron disease, 752
Ponies, hyperlipemia in, 701
Pool phase of musculoskeletal nuclear scintigraphy, 500
Poor exercise recovery in inflammatory airway disease, 413
Poor performance
and lower airway disease, 413
axial deviation of the aryepiglottic folds causing, 378-379
in racing horses with respiratory tract diseases, 408
nuclear scintigraphy screening for, 501
without overt signs of respiratory disease, 416-417
Porphyrins, 175

- Portable cooled cameras, 503
 Port-A-Cul, 155, 229
 Portals, 372
 Positive end-expiratory pressure (PEEP) valve, 652
 Positive flexion test, 498
 Post anesthetic neuropathies, 739-740
 Postanesthetic myasthenia syndrome
 differentiation of, 743t
 idiopathic, 740
 Postanesthetic upper respiratory tract obstruction, 391-393
 clinical signs of, 392
 etiology of, 391-392
 treatment of, 392-393
 Postantibiotic effect (PAE), 850
 Postbreeding endometritis, 278
 Posterior segment, examination of, 453-454
 Postexercise electrocardiogram, thoroughbred, atrioventricular block, 605f
 Postfoaling mare, colic in, 328
 Postganglionic fibers stimulated by acetylcholine, 109
 Posting trot, changing diagonals in, 497
 Postoperative colic, paralytic ileus in, 111
 Postoperative colic surgery patients, nutritional therapy of, 722-723
 Postoperative ileus (POI) complicating surgical colic, 108-109
 Postoperative management of the orthopedic patient, 544-546
 Postoperative respiratory noise complicating arytenoidectomy, 383
 Postpartum hemorrhage, 327-330
 clinical signs of, 329t
 emergency kit, 327-328, 328t
 emergency treatment of
 algorithm of, 329-330
 physical examination of, 327-328
 Postpartum mares
 endometrial culture in, 231
 evaluation of, 322-324
 Postpartum metritis, 105
 Potassium
 for acute renal failure, 843
 for congestive heart failure, 617
 for dehydration, 119, 156
 for hepatic failure, 172
 for renal tubular acidosis, 849
 in feed, 721t
 in forages, 721
 Potassium iodide for heaves, 420
 Potassium penicillin
 for arytenoid chondrosis, 382
 for jugular vein thrombophlebitis, 626
 for perinatal asphyxia syndrome, 648t
 for vasculitis, 365
 Potassium penicillin G
 for ocular emergencies, 463t
 for peritonitis, 156
 for retained fetal membranes, 332
 in NFDSM-G extender formulation, 267
 Potassium salts for anhidrosis, 817
 Potato bugs, 784
 Potomac Horse Fever. *See* Equine Monocytic Ehrlichiosis
 Potomac horse fever vaccine, 252
 Povidone-iodine, 479t
 for folliculitis, 200
 for ocular emergencies, 464t
 Povidone-iodine—cont'd
 for retained fetal membranes, 332
 for staphylococcal bacterial folliculitis, 198
 for uterine infection, 231
 Povidone-iodine shampoo, 199
 PPID. *See* Pituitary pars intermedia dysfunction (PPID)
 PPS. *See* Pentosan polysulfate (PPS)
 PQCT. *See* Peripheral quantitative CT scanners (pQCT)
 P:QRS ratio, 577
 Pralidoxime chloride for cutaneous habronemiasis, 305
 Praziquantel for intestinal tapeworm, 160
 Prebiotics, 27, 713-714
 commonly used, 712b
 Predict-A-Foal, 316
 Prednisolone
 for atopic dermatitis, 182-183
 for axial deviation of the aryepiglottic folds, 380
 for collagenolytic granuloma, 207
 for cutaneous habronemiasis, 196
 for equine recurrent uveitis, 471t
 for heaves, 418
 for pemphigus foliaceus, 218
 for photosensitivity, 176
 for sick neonatal foals, 640
 for sterile nodular panniculitis, 208
 for stiff horse syndrome, 763
 for upper airway disease, 399
 for urticaria, 206
 for vasculitis, 365
 Prednisone (Deltasone)
 for cutaneous lymphosarcoma, 211
 for heaves, 418
 for lymphoma, 361
 for pemphigus foliaceus, 218
 for plasma cell myeloma, 362
 for upper airway disease, 399
 for vasculitis, 365
 Predominant rhythm, determination of, 577
 Pregnancy
 endometrial cysts in
 therapy for, 231
 endotoxemia in, 108
 loss during late gestation, 297
 rate of, 248
 from frozen semen, 274t
 optimization of, 274-275
 termination with prostaglandin, 246
 with enlarged ovaries, 261
 Pregnant recipient mares, feeding of, 279
 Pregnant uterus, 293f
 Prekallikrein deficiency, 352-353
 Premature foals, 634
 and glucose, 643
 body temperature of, 643
 cardiopulmonary system of, 643
 clinical progression of, 642-643
 corticosteroids for, 644
 immune system of, 643-644
 laboratory data for, 642
 musculoskeletal system of, 643
 physical characteristics of, 641
 physical maturity of, 642
 prognosis of, 642
 reason for, 642
 Premature lactation
 and colostrum loss, 693
 in placentitis, 298
 Premature parturition causing retained fetal membranes, 330
 Premature placental separation, 633
 Prematurity, 641-644
 Premise sprays, 193, 193b
 Preoperative examination of foals, 689
 Preoperative management of the orthopedic patient, 544
 Prepartum maternal signs of fetal compromise, 631-632
 Prepartum treatment, 632-633
 Preperformance testing, 499
 Prepubic tendon
 rupture of, 310-311, 311f, 645
 causing dystocia, 320
 Prepurchase examination, 496-497
 close observation during, 495-496
 conformation, 493-495
 history in, 493
 imaging in, 497-498
 lesions in, 498
 nuclear scintigraphy during, 501-502
 of fore limb, 496
 of hindlimb, 496
 of horse in motion, 496-497
 orthopedic concerns in, 493-499
 palpation during, 495-496
 resting horse observation in, 493
 riding in, 497
 worksheet for, 493, 494f-495f
 Preputial trauma in breeding stallion, 303-304
 Pressure bandages for vasculitis, 365
 Pressure gradients, 579
 Prey-mentality, 455
 Priapism, 304-305, 304f
 Primarin in critical care, 21
 Primary muscle disorders, disorders causing, 741t
 Primiparous mares, perineal lacerations in, 333
 Probiotics, 27-28, 711-713
 clinical application of, 713
 commonly used, 712b
 mechanisms of action, 712b
 safety of, 713
 Procainamide
 for dysrhythmias, 604t
 for myocardial disease, 621
 for ventricular tachydysrhythmias, 611-612
 Procaine penicillin
 avoidance of, 745
 for jugular vein thrombophlebitis, 626
 for permanent tracheostomy in standing horses, 397
 for retained fetal membranes, 332
 for strangles, 67
 Processing form for semen shipments, 268
 Procollagen, 517
Procyon lotor. *See* Northern raccoon (*Procyon lotor*)
 Progesterone
 causing estrus onset delay, 249-250
 demonstrating placentitis, 299-300
 for cervical lacerations, 334
 for fetal compromise, 632
 for recipient mares, 278, 279
 from corpora lutea, 261
 Progestin from placenta, 261
 Progestogens
 for cutaneous lymphosarcoma, 210
 for endometrial cysts, 232
 for fetal compromise, 632
 Prognathia, 86f, 87
 Programmed cell death, 177
 Progressive anemia, 223

- Progressive borborygmi, 681
 Progressive ethmoid hematoma, 375-378
 clinical signs of, 375
 diagnosis of, 375
 prognosis of, 378
 signalment, 375
 treatment of, 376-377
 Prokinetic agents
 for ileus, 22t, 109-111
 in critical care, 21
 Proliferative enteropathy, 164-166
 clinical pathology of, 165
 clinical presentation of, 165
 diagnosis of, 165
 differential diagnosis of, 165
 prevention of, 165-166
 prognosis of, 165
 therapy of, 165
 Prolonged anestrus, 262
 Prolonged enteral feeding, 710
 Prolonged gestation, 633
 Proopiomelanocortin (POMC), 807
 Propafenone
 for dysrhythmias, 604t
 for ventricular ectopic beats, 611
 Propantheline bromide, 286
 for fetal gender determination, 288
 Proparacaine
 for direct ophthalmic examination, 462
 for ocular emergencies, 463t
 for ophthalmic examination, 451
 Prophylactic administration of sodium cromoglycate for heaves, 420
 Propiomazine for penile paralysis, 304
Propionibacterium acnes, 39, 446, 673
 Propofol, 18-19
 for foals, 689-690
 Propranolol
 for dysrhythmias, 604t
 for ventricular tachydysrhythmias, 612
 Prostaglandin
 causing corpus luteum regression, 249
 for pregnancy termination, 246
 for recipient mares, 279
 Prostaglandin analogues for gastric ulcers, 98
 Prostaglandin E2 (PGE2), 558-559
 and cervical relaxation, 316
 Protein bumps, 206
 Protein C deficiency, 353
 Protein, equations for, 716b
 Protein:energy ratio, 698
 requirements of
 in acutely ill horse, 707
 Proteins, 698
 Proteinuria, 821
 Proteoglycans, 26
 Prothrombin time (PT), 171
 Proton density (PD), 509
 Proton pump inhibitor for gastric ulcers, 98
 Protozoal agents causing interstitial pneumonia, 425
 Protozoan parasites with foal diarrhea, 678
 Proximal enteritis, 120
 diagnosis of, 150
 Proximal intertarsal joint, degenerative joint disease of, 541
 Proximal nasolacrimal system, stenosis of, 490
 Proximal sesamoid bones, lesions of, computed tomography of, 506
 Pruritus, 181
 associated with mite infestations, 189
Pseudomonas, 4, 465, 838
 in semen, 255
Pseudomonas aeruginosa, 6, 10, 11
 causing placentitis, 297
 causing retained fetal membranes, 330
 complicating burns, 224
 in foal pneumonia, 666
 Pseudothrombocytopenia, 349-350
 Pseudotruncus arteriosus, 600
 PSGAGs. *See* Polysulfated glycosaminoglycans (PSGAGs)
Psorophora, 48
Psoroptes, 187, 189
Psoroptes equi, 187
Psoroptes mites, 190
Psoroptes natalensis, 187
Psoroptes ovis, 187
 Psoroptic ascariasis, 187
 PSSM. *See* Polysaccharide storage myopathy (PSSM)
 Psychogenic polydipsia, 822, 830-831, 830f
 Psyllium, 724
 for cecal impaction, 140
 for dehydration, 119
 for right dorsal colitis, 142
 PT. *See* Prothrombin time (PT)
 Ptosis, 462
 secondary to neurologic disease, 476
 Pulmonary alveolar macrophages (PAM), 404-405
 Pulmonary artery, origin of, 592
 Pulmonary atresia, 600
 with ventricular septal defect, 600
 Pulmonary capillaries, disruption of, 430
 Pulmonary capillary transmural pressure, determination of, 430
 Pulmonary consolidation, fluid bronchogram of, 422f
 Pulmonary edema, 574
 Pulmonary emphysema, 793
 Pulmonary eosinophilia, 410
 Pulmonary function tests, 415
 Pulmonary hypertension, two-dimensional echocardiography, 617f
 Pulmonary outflow velocity, Doppler echocardiography, 581f
 Pulmonary thromboembolism, diagnosis of, 627
 Pulmonic regurgitation, 619
 Pulmonic valve, auscultation of, 575
 Pulse
 monitoring thoracic compressions in foal, 654
 quality of in cardiovascular examination, 573
 Pulse oximetry for foals, 691
 Pulsed dye laser fragments calculi, 834
 Pulsed-wave Doppler, 579
 for aortic aneurysms, 624
 for aortic regurgitation, 618
 for jugular vein thrombophlebitis, 626
 for regurgitant jet, 617
 of mitral valve, 616
 Punkies, 191
 Pupillary light reflex (PLR)
 in cardiopulmonary resuscitation of foals, 654
 tests, 451-452
 Pupils
 constriction of, 474, 478
 differences in size of, 452
 Purple bacteria, 74
 Purpura hemorrhagica, 363
 treatment of, 67
 with penile paralysis, 304
 Purpura in vasculitis, 364
 Purulent odor discharge, 490-491
 Pustules, 217
 Pyelonephritis, 835
Pyemotes tritici, 189
Pyemotes ventricosus, 189
 Pyloric sphincter, 101
 Pyloric stenosis, weanling with, 102f
 Pyloric ulcer in foals, 96
 Pylorus, 101
 Pyrantel embonate for intestinal tapeworm, 159
 Pyrantel pamoate
 cyathostomiasis resistance to, 162, 163
 for cyathostomes, 162
 Pyrantel tartrate
 cyathostomiasis resistance to, 163
 for intestinal tapeworm, 159
 Pyrethroid-based insecticide/repellent, 191
 Pyrethroids for equine pastern dermatitis, 203
 Pyrexia, 153
 with equine viral arteritis, 364
 Pyrillamine maleate
 for arthropod hypersensitivity, 185
 for atopic dermatitis, 183
 Pyrimethamine, 29
 for equine protozoal myeloencephalitis, 72-73
 Pyrrolizidine alkaloid, 675
 plants with, 175b
 poisoning, 779, 788-790
 toxicity, 171-172
 toxicosis, 173
 Pyrrolizidine causing interstitial pneumonia, 426
 Pyrrolizidine-containing plants, 768
Q
 QRS, 577, 602
 Quadrisol. *See* Vedaprofen (Quadrisol)
 Quarantine, 24-25
 Quarter Horse-related breeds , polysaccharide storage myopathy in, 733
 Quarter Horses
 glaucoma in, 486
 hemophilia A in, 351
 hyperelastosis cutis in, 219
 linear alopecia in, 216
 midpalmar pastern, T2-weighted image of, 510f
 multiple myeloma in, 362
 racing, 429
 sarcoïd in, 484
 selective immunoglobulin M deficiency in, 696
 sodium hyaluronate for, 560
 Quaternary ammonium compounds, 25
 Quick-setting urethane, 525
 Quiescent macrophages, 228
 Quinidine
 for aortocardiac fistulas, 625
 for atrial fibrillation, 608-609
 complications of, 607-608
 for dysrhythmias, 604t
 for ventricular tachydysrhythmias, 611
 side effects of, 608t

R

- RAAS. *See* Renin-angiotensin activating system (RAAS)
- Rabies, 758, 766
inactivated vaccines for, 770-771
with penile paralysis, 304
- Racehorses
Adequan for, 561
axial deviation of the aryepiglottic folds in, 379
fetlock joint of, 501
MAP-5 for, 555
nuclear scintigraphy in, 500
poor performance in with respiratory tract diseases, 408
radiography of in prepurchase examination, 498
screening scintigraphy in, 501
stress fractures in, 500
with cough, diagnostic approach to, 415
with equine protozoal myeloencephalitis, 70
- Racing, drug testing in, 32-35
- Radial immunodiffusion (RID), 693
- Radial nerve, damage to, 735
- Radial pressure wave therapy, 562-564
- Radiation, 503
- Radiofrequency hyperthermia, 484
- Radiography
for cardiovascular disease, 584
for fractured ribs, 436
in prepurchase examination, 497-498
of angular limb deformities, 664
of cauda equina damage, 758
of digital flexor apparatus contracture, 534
of guttural pouch mycosis, 389
of nasal passages, 370-371
of premature foals, 634
of progressive ethmoid hematoma, 375
of urinary tract, 823
with thermography, 504
- Radioimmunosorbent assay (RIA), 182
- Radiolabeled aerosol, 439
- Rain scald, 198
- Ramps, 84-85
- Range of motion, 497
- Ranitidine (Zantac)
for gastric ulcers, 98
for perinatal asphyxia syndrome, 648t
- RAO. *See* Recurrent airway obstruction (RAO)
- Rare-earth screens, 370
- Rattlesnakes (*Crotalus* spp.) causing intravascular hemolysis, 345
- Rayless goldenrod, 783
- RDS. *See* Respiratory distress syndrome (RDS)
- Reactive oxygen metabolism, 136
- Real time B echocardiography, 578
- Rear legs, magnetic resonance imaging of, 508f
- Recipient mares, 278-279
- Reciprocating blades, 82
- Recombinant human erythropoietin (Epoen), 343
- Recombinant tissue plasminogen activators for thromboembolism, 627
- Rectal examination
for large colon impaction, 132
for lower motor neuron disease, 752
prior to endometrial sampling, 229
structures identified during, 129f
in ileal impaction, 129f
- Rectal mucosa, palpating, 151
- Rectal palpation
for fetal compromise, 632
for fetal gender determination, 288
for placental hydrops, 301
for recipient mares, 278
risk of, 151
- Rectal prolapse, 325
- Rectal tears, 150-153
classification of, 151t
client communication about, 152
complications of, 151
diverting loop colostomy in, 153f
emergency treatment of, 152
initial management of, 151
liability of, 151
nutritional therapy of, 726
severe, treatment of, 152-153
transrectal endoscopic view of, 151f
- Rectourethral fistulas, 828
- Rectovaginal fistulas, 828
- Rectus capitis ventralis muscle, rupture of, resembling progressive ethmoid hematoma, 375
- Recurrent airway obstruction (RAO), 417-421, 793-794
acute episodes of, 417-420
aerosolized treatment of, 440-444
monitoring response to, 441
patient nonresponse to, 444
sample regimens for, 444-445
definition of, 412
- Recurrent exertional rhabdomyolysis (RER), 727, 728
potential rations for, 732t
recommended diets for, 731-733
- Recurring iridocyclitis, 468-473
- Red bad delivery, 633
- Red blood cells
transfused, 355
velocity of, 579
- Red clover poisoning, 790-791
- Red fox, 187
- Red maple toxicity, 344
- Reflex lacrimation, 490
- Refractive state affecting visual acuity, 456
- Regional anesthesia, nuclear scintigraphy after, 500-501
- Regulatory issues associated with intraarticular corticosteroids for competing horses, 554
- Rejected foals, nurse mares for, 265
- Relative polycythemia, 358
- Relaxin demonstrating placentalitis, 300
- Relay toxicity, 783
- Renal agenesis, 827
- Renal arteriovenous malformation, 828
- Renal biopsy, 823, 847
- Renal blood flow, increase of, 843
- Renal cysts, 827
- Renal dysplasia, 827
- Renal failure, 718-719
acute. *See* Acute renal failure
chronic. *See* Chronic renal failure
- Renal hematuria, idiopathic, 855-856
- Renal hypoplasia, 827
- Renal tubular acidosis (RTA), 848-850
- Renal ultrasonography, 847
for acute renal failure, 842
- Renal vascular anomalies, 855-856
- Renin-angiotensin activating system (RAAS), 611
- Repeated abdominocentesis, 297
- Repellents, 193b
- Reperfusion injury, 135-137
in large colon, 136
- Reproductive history of donor mares, 277, 278
- Reproductive system
molds in, 792
of mare, examination of, 272
- Reprolapse, 325
- RER. *See* Recurrent exertional rhabdomyolysis (RER)
- Reservoirs, 24
- Resistant bacteria, 6-7
- Resistant cyathostomiasis, 161-165
definition of, 161-162
diagnosis of, 161-162
population dynamics of, 161
treatment of, 163-164
- Respiratory acidosis, 643
- Respiratory disease, 38-39
immunomodulators in, 445-448
- Respiratory distress syndrome (RDS)
neonatal, 643
- Respiratory sinus arrhythmia, 604
- Respiratory sinus arrhythmia, ambulatory echocardiography of
thoroughbred horses, 605f
- Respiratory stridor, 773
- Respiratory syndromes, conjunctivitis associated with, 475
- Respiratory viral infections,
bronchoalveolar lavage, 411
- Resting arrhythmias, 587
- Resting base-apex echocardiography from
thoroughbred horses, 578f
- Resting echocardiography, 589
- Resting horse
examination of in upper airway disease, 366-368
observation of in prepurchase examination, 493
- Resting 24-hour continuous electrocardiograms (Holter monitor)
for aortic regurgitation, 618
- Restlessness
in postpartum hemorrhage, 328
in uterine torsion, 312
- Restraint
during artificial insemination, 273
for ophthalmic examination, 451
- Resuscitation bag, 652
- Retained fetal membranes (RFM), 330-332
diagnosis of, 330-331
etiology of, 330
incidence of, 330
pathogenesis of, 330
prognosis of, 332
treatment of, 331-332
- Retention sutures for penile trauma, 303
- Retina
detachment of, 467
ganglion cells in, 486
hemorrhage of secondary to neurologic disease, 476
- Retinoids for cutaneous lymphosarcoma, 211
- Retroillumination, 475
- Retropharyngeal lymph nodes,
Streptococcus equi abscesses of, 398
- Reverse shoe, 525
- RFM. *See* Retained fetal membranes (RFM)
- Rhabdomyolysis, thoroughbreds with, 733
- Rhinopneumonitis vaccine, 252

- Rhinopneumonitis viruses, 305-306
Rhizobium, 107
Rhizopus, 792
Rhodobacter sphaeroides, 107
Rhodococcus equi, 6, 838
 causing enteritis, 167
 causing interstitial pneumonia, 426
 causing pneumonia, 166-167, 171
 immunization for, 357
 causing purpura hemorrhagica, 363
 causing weanling diarrhea, 165
 in foal diarrhea, 679
 in foal pneumonia, 666-674
 epidemiology of, 667
 pathogenesis of, 667-668
 prevention of, 673-674
 treatment of, 671
 with acute respiratory distress syndrome, 675
Rhodococcus equi infections, 60-63
 clinical manifestations of, 60-61
 diagnosis of, 61
 early recognition of, 63
 passive immunization, 63
 pathogenesis of, 60
 prevention of, 62-63
 prognosis of, 62
 treatment of, 62
Rhododendron, 783
 RIA. *See* Radioimmunosorbent assay (RIA)
 Rice bran, 733
 fat content of, 731
 RID. *See* Radial immunodiffusion (RID)
 Riddell's goundsel, 789
 Riding in prepurchase examination, 497
 Rifampin
 for equine monocytic Ehrlichiosis, 77
 for foal pneumonia, 671
 for *Rhodococcus equi* infections, 62
 neonatal metabolism of, 3
 Right arm electrode, 602
 Right atrium, enlargement of, 614
 Right dorsal colitis, 141-143, 724-725
 clinical signs of, 141
 diagnosis of, 142
 signalment of, 141
 therapy of, 142-143
 ultrasonographic image of, 142f
 Right leg electrode, 602
 Right ventricle, echocardiography of, 582f
 Right ventricular outflow tract (RVOT)
 view, 580
 Right-to-left shunt, 594
 Rimadyl. *See* Carprofen (Rimadyl)
 Rimantadine hydrochloride for equine influenza, 43
 Ringer's solution for large colon impaction, 133
 Ristocetin cofactor activity for von Willebrand's disease, 352
 Roach back, 495
 Roberts, Monty, 570
 Rodenticides causing hemorrhagic diathesis, 354
 Roferson-A. *See* Interferon alpha-2a (Roferson-A)
 Rolling mare for uterine torsion, 313
 Romifidine, 17
 Ronnel for skin parasites, 196
 Root, granular pattern around, 374
 Rose Bengal dye, 451
 for fungal keratitis lesions, 478
 inhibiting herpesviruses, 475
 Rostral hooks, 84, 84f
 Rostral maxillary sinus, portals for, 372
 Rostral ramps, 84f
 Rotavirus
 causing enteritis, 167
 causing weanling diarrhea, 165
 Rowdy breeding behavior, 318
 RR-interval, 578f
 RTA. *See* Renal tubular acidosis (RTA)
 Rubber pressure bandage for penile trauma, 303
 Ruptured bladders in foals, 681
 Ruptured viscus, 149
 Russian knapweed, 781-782
- S**
 Sabouraud's dextrose medium, 478
 Sabulous urolithiasis, 833
Saccharomyces boulardii, 168
Saccharomyces cerevisiae, 28, 714
 Sacrocaudalis dorsalis medialis muscle, biopsy of, 744
 Sacrococcygeal vertebral osteomyelitis, 756-757
 Sacroiliac pain, 496
 Saddle
 bruising, 495
 proper fit of, 570
 SADMOAs. *See* Slow-acting disease-modifying agents (SADMOAs)
 Safflower oil, 724
 Sagittal ratio, 748f
 Salbutamol, 437
 for anhidrosis, 817
 Saline agglutination test, 355
 Saline for guttural pouch empyema, 387
 Salinomycin intoxication, 620
 Salmeterol
 for heaves, 419
 for recurrent airway obstruction, 444
Salmonella colitis, 105
Salmonella infection, 56-59
Salmonella typhimurium, 838
 in neonatal septicemia, 660
 Salmonellae, 10
 causing weanling diarrhea, 165
 Salmonellosis, 56-59
 bacterial culture of, 58
 clinical signs of, 57
 diagnosis of, 57-58
 enzyme-linked immunosorbent assay of, 58
 epidemiology of, 56-57
 immunization for, 357
 in foals, 679
 nomenclature of, 56
 pathophysiology of, 57
 polymerase chain reaction, 58
 prevention of, 59
 treatment of, 58-59
 Sample handling of tracheal aspirates, 403
 Sand colic, 724
 Sand flies, 191
 Sanitation, 24
Sarcocystis neuroma, 69
Sarcocytes neuroma, 752, 756
 Sarcoid, 484-485
 prognosis of, 481t
Sarcoptes scabiei equi, 187
 Sarcoptic ascariasis, 187
 Sarcotiforms, 189
 Sauerkraut poultice for equine pastern dermatitis, 202
 Sawhorse stance in uterine torsion, 312
 Scalding, 221
 Scanners, 505-506
- Schirmer tear test (STT), 452, 474, 475, 476
 Schoolmasters, diastolic murmurs in, 573
 SCID. *See* Severe combined immunodeficiency (SCID)
 Scintigraphy with thermography, 504
 Sclera
 perforation of, 464
 rupture of, 464
 slit lamp biomicroscope examination of, 450
 Scleral lamina cribrosa, 486
 Sclerotic, 796
 Scoliosis, 495
 Scopalamine for large colon impaction, 133
 Scratches, 201-203
 Screws for valgus and varus deviations, 665
 Scrotal hernia, 307, 307f
 examination for, 306
 SDF. *See* Superficial digital flexor (SDF)
 SDH. *See* Sorbitol dehydrogenase (SDH)
 Seasonal familial hypersensitivity syndrome, 193
 Seasonal variation of hypothalamic-pituitary-testicular axis, 258
 Seasonality and dopamine antagonist, 239
 Second heart sound (S2), 575
 Secondary screwworm, 194
 Second-degree atrioventricular block, 603-604
 Second-degree burns, 220
 Sedation
 for tracheal aspiration, 402
 in forebrain disease, 769
 of foals, 688-691
 Sedatives, 17-18
 for colic, 116t, 117
 for colic in foals, 686
 for ileal impaction, 128
 for neonates, 5
 Segmental myelitis, 69
 Seizures, 764-765, 771
 neonatal, 5
 Selective immunoglobulin M deficiency, 696
 Selenium
 for cervical stenotic myelopathy, 748
 for exertional rhabdomyolysis, 730
 natural history of, 801
 Selenium deficiency, 620
 Selenium toxicity, 801-804
 diagnosis of, 803-804
 management, 804
 pathophysiology of, 801-802
 prevention, 804
 therapy, 804
 Selenosis, 802
 Self-biting, 319
 Self-mutilation, 318-319
 Self-tolerance, failure of, 346
 Semen
 bacterial contamination of, 255-256
 collection area for, 253-254
 collection of, 253-254, 266-267
 cryopreservation of, 269-271
 deposition of in artificial insemination, 274f
 extender of, 253, 267
 ground collection of, 254
 interstate shipment of, 266
 liquid preservation of, 266-269
 pathogens in, 253

- Semen—cont'd
 preservation of, 266-267
 quality of, 253
 storage of, commercial systems for, 267-268
 transportation of
 commercial systems for, 267-268
 processing form for, 268
 urine in, 255
- Seminal plasma, abnormal, 256
- Seminoma, 308f
 of testicles, 308
- Senecio*, 426, 768, 788
Senecio flaccidus, 789
Senecio jacobae, 789
Senecio riddellii, 789
Senecio vulgaris, 789
Senna obtusifolia, 782
Senna occidentalis, 782
- Sensitivity, definition of, 503
- Sensory cutaneous area of pectoral and thoracic limb regions, 737f
- Sensory loss, 773
- Sensory nerve evaluation, 736-738
- Sepsis, 831
 in neonatal foal, 633-634
 in premature foals, 642
 neonatal, 3-4
 signs of, 657
- Septic arthritis, 61
 in neonates, 657
 therapy of, 660-661
 in septic foals, 657
- Septic joint, arthrocentesis of, 658
- Septic jugular vein thrombophlebitis with tricuspid endocarditis, 614
- Septic peritonitis, 105
 prognosis of, 157-158
 surgery of, 157
- Septic pneumonia resembling progressive ethmoid hematoma, 375
- Septic thrombophlebitis, 626
- Septicemia, 469, 793
 neonatal. *See* Neonatal septicemia
 recognition of in neonatal septicemia, 656-658
- Septum primum, 592f
- Serapin for upward fixation of the patella, 536
- Serologic diagnosis
 of equine protozoal myeloencephalitis, 72
 of tapeworm infection, 159
- Serologic testing, 474
- Seromucoid gland of nictitating membrane, 488
- Serous ocular discharge, 489-490
- Sertoli's cell tumors of testicles, 308
- Serum albumin for cryopreservation, 282
- Serum allergy test for atopy, 181-182
- Serum anti-P2 antibodies with cauda equine neuritis, 758
- Serum biochemistry, urinalysis, 820
- Serum, biomarker sampling, 514
- Serum calcium in cantharidin toxicosis, 785
- Serum copper and vessel fragility, 327
- Serum creatinine in premature foals, 634
- Serum insulin concentration for pituitary pars intermedia dysfunction, 810
- Serum magnesium in cantharidin toxicosis, 785
- Serum neutralization test, 52
- Serum selenium, 803-804
- Serum T4 (thyroxine) test, 250
- Serum vitamin E and chronic exertional rhabdomyolysis, 729
- Sesamoid apex, large enthesiophytes of, 498
- Sesamoid fractures, 498
- Sesamoidean ligaments, magnetic resonance imaging of, 509
- Sesamoiditis, 499
- Setaria*, 767
Setaria digitata, 775
Setaria lutescens (yellow bristle grass), 89
- Severe combined immunodeficiency (SCID), 696
- Severe equine rhabdomyolysis, 743t
- Severe hemorrhage, 340
- Sevoflurane, 690
- Sex chromosomes, absence of, 261
- Sex determination, 288
- SGAG. *See* Sulfated glycosaminoglycans (sGAG)
- Shaker foal syndrome, 740
- Sharp enamel points, 82
- Sharp trauma, global rupture, 464
- Sheared heels
 acquired, 529
 conformation, 529
 corrective shoeing of, 530-531
 diagnosis of, 530
 etiology of, 529-530
 in foals, 529
 palmar view of, 529f
 plantar view of, 529f
 prognosis of, 531
 shoeing management of, 528-532
- Shims, 525
- Shipped semen
 artificial insemination with, 271-272
 stallion selection for, 271-272
- Shivering, 762
- Shivers, 499
- Shock, 225
 in small intestine strangulating obstruction, 124
- Shock wave fields
 energy flux density within, 564
- Shock waves
 cellular stimulation, 564f
 effect in tissue, 564-565
 generation of, 562-563, 563f
 graphic representation of, 563f
 physical properties of, 562-563
- Shoeing, improper, 529-530
- Shoes
 glued on, 525-526
 in laminitis, 523-524
 too small, 530f
- Short axis echocardiogram from right side, 582f
- Short-acting bronchodilator drugs, 441-442
- Shoulder flexion, 321
- Shoulder lock, 320
- Show horses
 Adequan for, 561
 with inspiratory noise
 without exercise intolerance, 384-385
- Show jumping, 429
 navicular pain with, 498
- Show-shoe hare encephalitis, 766
- Shredded paper, 420
- Shunting, identification of, 600
- Shunts, clinical pathophysiology of, 594-595
- Sidebones, ossification of, 498
- Signalment
 cardiovascular examination, 573
 cranial nerve diseases, 776
- Silent ovulation, 264
- Silicone putty, 526
- Silvadene. *See* Silver sulfadiazine (Silvadene)
- Silver adhesive electrodes, 576
- Silver sulfadiazine (Silvadene)
 for electrical burns, 224
 for ocular emergencies, 464t
 for thermal burns, 222
- Simian immunodeficiency virus, 45
- Simulium*, 184, 191
- Single radial hemolysis (SRH) tests, 44
- Single-pulse gonadotropin-releasing hormone challenge test, 258-259
- Sinoatrial block, 604
- Sinus cysts, diagnosis of, 374
- Sinus diseases, diagnosis of, 369-374
- Sinus of Valsalva, 624
- Sinus rhythm, echocardiogram, 603f
- Sinuses
 percussion of, 369
 trephine site, 372f
- Sinusitis, diagnosis of, 373
- Sinusotomy, 376
- SIRS. *See* Systemic inflammatory response syndromes (SIRS)
- Sistrurus* sp. *See* Pigmy rattlesnakes (*Sistrurus* sp.)
- Skeletal muscle weakness, disorders causing, 741t
- Skeletal tissue turnover, body fluid biomarkers, 515t
- Skin
 maceration of, 303
 molds in, 792
 thermography of, 503
- Skin biopsy
 for atopy, 181
 for cutaneous adverse drug reactions, 178
- Skin creams for penile trauma, 303
- Skin diseases, 174-176
 congenital, 219
- Skin grafting, 223
- Skin parasites, elimination of, 196-197
- Skin scrapings of mite infestation, 190
- Skin-So-Soft, 185
- Skip biopsies, histopathologic examination of, 218
- Skull
 computed tomography of, 506
 fracture of, diagnosis of, 374
 lateral radiographs of, 371
 sinus mass in, computed tomography, 507f
- Slide preparation of tracheal aspirates, 403
- SLIE. *See* Systemic lupus erythematosus (SLE)
- Sling for lower motor neuron disease, 753
- Slit lamp
 for vitreous humor examination, 453
 in cornea examination, 453
- Slit lamp biomicroscope, 450
 for anterior chamber examination, 453
- Slow-acting disease-modifying agents (SADMOAs), 15, 26-27
- Small airway (bronchiolar) inflammation, 407
- Small colon mesentery, rupture of, 325-326
- Small inactive ovaries, 261

- Small intestine
 epiploic foramen entrapment of, 125-126
 imaging of, 148
 intussusception of, 149
 strangulation obstruction of, 148
 strangulation of, 150
- Small intestine strangulating obstruction, 124-126
 causes of, 125-126
 clinical signs of, 124
 postsurgical complications of, 126
 prognosis of, 126
 treatment of, 124-125
- SMLN. *See* Submandibular lymph nodes (SMLN)
- Smoke inhalation, 224
 causing interstitial pneumonia, 426
- Snail (*Elimia livescens*), 75
- Snail (*Juga yrekaensis*), 75
- Snakebites causing intravascular hemolysis, 345
- Snare rod, 320
- Snellen fraction, 456
- Snip biopsy, 474
- Snybiotics, 714
- Sodium
 and readiness for birth, 315
 for retained fetal membranes, 332
 in feed, 721t
- Sodium bicarbonate
 for cardiopulmonary resuscitation of newborn foal, 653
 for chronic renal failure, 847
 for myasthenia, 745
- Sodium chloride
 detection of tapeworm eggs, 158-159
 for chronic renal failure, 847
- Sodium cromoglycate (Intal)
 for recurrent airway obstruction, 443
 prophylactic administration of for heaves, 420
- Sodium gluconate for thromboembolism, 627
- Sodium hyaluronate (hyaluronan)
 corticosteroids with, 553
 for joint disease, 560
- Sodium hypochlorite for folliculitis, 200
- Sodium pentosan polysulfate (NaPPS), 557
- Soft palate
 displacement of, 367f, 398-399
 dorsal displacement of
 causing postanesthetic upper respiratory tract obstruction, 391
 treatment of, 392
- Soft tissue injuries, around joints,
 magnetic resonance imaging of, 509
- Soft tissue phase of musculoskeletal nuclear scintigraphy, 500
- Solganal. *See* Aurothioglucose (Solganal)
- Solid PVC splints for incomplete ossification of cuboidal bones, 664
- Solitary plasmacytoma, 361
- Sorbitol dehydrogenase (SDH), 169, 176
- Sorghum-sudan grass toxicity, 756
- South America, stringhalt in, 761
- Southeastern United States, ileal impaction in, 127
- Soy oil
 providing calories, 718
 supplements
 for colitis, 724
- Soybean meal, mineral content of, 721t
- Spanish fly beetles, 784
- Spasmodic colic, prevention of, 160
- Speculum, 82
 examination of perineal lacerations, 333
- Sperm
 heat shock to, 254
 low numbers per ejaculate, 256
 membranes
 floctometric analysis of, 272
 number of, 268
 stasis, 256
- Spermatic cord, torsion of, 308-309
 surgery of, 309f
- Spermatozoa
 environmental sensitivity of, 266
 glucose substrates for, 267
 testing ability to survive cooled storage, 266-267
- Spinal accessory nerve, biopsy of, 744
- Spinal cord diseases, 750-753
 signs of, 70
- Spinal cord trauma, 749
- Spinal injuries with penile paralysis, 304
- Spinal reflex testing, 751t
- Spinal tap, 752
- Spine, computed tomography of, 507
- Spin-echo imaging, 509-510
- Spiral scanners, 505
- Spleen
 imaging of, 149
 penetration of, 154
- Splenectomy for thrombocytopenia, 350
- Spoiled gradient echo technique, 509
- Spontaneous middle uterine artery hemorrhage, 340
- Sporadic abortions, 474
- Sporadic exertional rhabdomyolysis, 727
- Sporanox. *See* Itraconazole (Sporanox)
- Sporothrix schenckii*, 213
- Sporotrichosis, 213-214
- Sport horses
 carpal joint disease in, 498
 inflammatory airway disease
 clinical signs of, 413
 diagnosis in, 416
 prepurchase examination of, 493
 suspensory branch lesions in, 498-499
 with exercise intolerance, 416-417
- Spotted blister beetles, 784
- Spring-loaded biopsy instrument, 260
- Sprinting racehorses, superficial digital flexor tendinitis in, 499
- Sputolysin. *See* Dembrexine (Sputolysin)
- Sputolysin for foal pneumonia, 672
- Squamous cell carcinoma, 474, 480-485
 clinical signs of, 480
 diagnostic methods of, 482
 differential diagnosis of, 480-483
 of bladder, 836
 of external genitalia, 836
 of penis, 305
 prognosis of, 481t, 482
 risk factors for, 480
 treatment of, 482-483
- Squinting, 478
- SRH tests. *See* Single radial hemolysis (SRH) tests
- St. John's Wort, 174
- St. Louis encephalitis, 766
- Stable flies, 186, 193, 305
- Stabling, 99
- Stack full-limb bandage, 548f
- Stall rest for laminitis, 522
- Stalled, 99
- Stallionlike behavior
 in geldings, 319
- Stallions
 artificial breeding of, 252-256
 general health considerations, 252-253
 behavior problems in, 317-319
 dependence, 269
 evaluation of prior to semen collection, 269
 fertility prediction of, 272
 inadequate libido of, 317-318
 rectal tears of, 151
 selection of for artificial insemination, 271-272
- Stand for breeding, failure to, 264
- Standardbred horse, 429
 harness fit in, 570
 hypervolemia in, phlebotomy for, 433
 recurrent exertional rhabdomyolysis in, 728
- Standing flank laparotomy for uterine torsion, 313-314, 314f
- Standing horses
 permanent tracheostomy in, 396-398
 ventricular premature depolarization in
 electrocardiogram, 588f
 with surgical ablation of progressive ethmoid hematoma, 376
- Staphylococcal bacterial folliculitis, 197-198
- Staphylococcus*, 4, 197, 838, 851
 in foals, 3
- Staphylococcus aureus*, 6, 197-198
 causing thromboembolic events, 620
 complicating burns, 224
 in jugular vein thrombophlebitis, 626
- Staphylococcus hyicus*, 197-198
- Staphylococcus intermedius*, 197-198
- Staples for valgus and varus deviations, 665
- Starches, 698, 717
 recommendations for, 703
- Static compression, 747
- Steeplechase racehorses, prepurchase examination of, 493
- Steeplechase racing, 429
- Stereopsis, 455
- Steric exclusion, 555
- Sterile canine urinary catheter, 154
- Sterile dressing, 550
- Sterile nodular panniculitis, 207-208
- Steroidogenic pathway, 261-262
- Steroids
 for thrombocytopenia, 350
 stimulating erythropoiesis, 343
- Stevens-Johnson syndrome, 177
 histopathology of, 178-179
- Stickers, 530
- Stiff horse syndrome, 762-763
- Stifle
 palpation of, 496
 radiography of, 498
 soreness in athletic horses, 499
- Stockin up, 787
- Stomach
 capacity of, 118
 imaging of, 148
 of foal, gastroscopic image of, 685f
- Stomach pump, 710
- Stomoxys calcitrans*, 184, 186, 193
- Strabismus, secondary to neurologic disease, 476
- Strangles, 64-68
 clinical signs of, 64
 diagnosis of, 64-65

- Strangles—cont'd
 epidemiology of, 65-66
 etiology of, 64
 outbreak control, 66
 prevention of, 68
 treatment of, 66-68
 vaccine, 252
- Strangulating lipoma, 125
- Strangulating obstruction
 of small intestine, 124-126
 vs. ileal impaction, 127
- Strangulating volvulus of ascending
 colon, 135
- Straw itch mite, 189
- Straw, substitutes for, 420
- Straws for frozen semen, 269-270
- Streptococcus*, 6, 10, 197, 838
 in foals, 3
 in jugular vein thrombophlebitis, 626
- Streptococcus equi*, 38, 64, 469, 838
 abscess of, 383-384
 abscesses of retropharyngeal lymph
 nodes, 398
 causing purpura hemorrhagica, 363
 causing thromboembolic events, 620
 complicating burns, 224
 in foal pneumonia, 666
 transmission of, control of, 67t
- Streptococcus pneumoniae* in thoroughbred
 racehorses, 414
- Streptococcus thermophilus*, 711
- Streptococcus zooepidemicus*, 42, 65
 causing placentitis, 297
- Streptokinase for thromboembolism, 627
- Stress, 95
 insulin insensitivity, 813
- Stress fractures
 definition of, 500
 extracorporeal shock wave therapy for,
 566
 in racehorses, 500
- Stress-induced disease, computed
 tomography of, 506
- Stretching, 569
- Stringhalt, 735, 760-762
 causes of, 739
- Striped beetles, 784
- Striped skunk (*Mephitis mephitis*), 69
- Stroma, abscess of, 466
- Strongyloides westeri*, 164
 causing enteritis, 167
 with foal diarrhea, 678
- Strongylus*, 767
- Strongylus vulgaris*, 758, 775
 in thromboembolism, 626-627
 larvae, 128
- STT. *See* Schirmer tear test (STT)
- Stylet, 402
- Stylohyoid fractures, computed
 tomography of, 507
- Styrofoam, 526
- Subarterial ventricular septal defects
 (VSD), 596
- Subchondral bones, contusions of,
 imaging of, 509
- Subchondral stress, magnetic resonance
 imaging of, 509
- Subconjunctival injection, 459
- Subconjunctival microosmotic pumps,
 459-460
- Subepiglottic cysts, laser surgery of, 395
- Subfertile stallions
 endocrine diagnostics of, 257-260
 human chorionic gonadotropin
 challenge, 259
- Subfertile stallions—cont'd
 hypothalamic-pituitary-testicular axis
 of, 258, 258f
 paracrine/autocrine testicular factors
 events occurring after initial decline
 in, 258f
 pituitary responsiveness assessment of,
 258-259
 testicular responsiveness assessment of,
 258-259
- Subischial urethrotomy for cystic calculi,
 833
- Submandibular lymph nodes (SMLN), 64
- Submandibular lymphadenopathy, 375
- Subpulmonic ventricular septal defects
 (VSD), 596
- Substance P as neurotransmitter, 109
- Subthalamus, 764
- Subtle seizures, 646
- Succinylcholine for bilateral laryngeal
 paralysis, 392
- Suck reflex, 661
- Sucralfate (Carafate)
 for *berteroa incana* toxicosis, 788
 for esophageal obstruction, 93
 for gastric ulcers, 98
 for neonatal gastric ulcers, 5
 for perinatal asphyxia syndrome, 648t
 for right dorsal colitis, 142
 oral administration of, 7
- Sucrose
 for cryopreservation, 282
 solution detection of tapeworm eggs,
 159
- Suction for pneumothorax, 434
- Sugars, 698, 717
- Sulfadiazine, 29
- Sulfamethoxazole
 for cystitis, 838
 for incontinence, 825
 for pleuropneumonia, 424
- Sulfasalazine for right dorsal colitis, 143
- Sulfated glycosaminoglycans (sGAG),
 514-515
- Sulfonamides
 dosage optimization of, 9
 for choledocholithiasis, 172
 for equine protozoal myeloencephalitis,
 72-73
 for foal pneumonia, 672
 for postpartum hemorrhage, 330
 neonatal metabolism of, 3
- Sulfonamide-trimethoprim for brainstem
 disease, 777
- Sulfur
 in feed, 721t
 shampoo, 199
- Sulpiride
 and seasonality, 239
 for ergopeptide alkaloid toxicosis,
 798
- Summer sores, 195-197, 305
- Sunburn, 220
- Sunburn cells, 176
- Superficial digital flexor (SDF)
 desmopathy of, 499
 palpation of, 496
 tendinitis of, 499
- Superior check ligament, palpation of,
 496
- Supplemental progestin therapy, 248
- Support foam, 550
- Supracristal ventricular septal defects
 (VSD), 596
- Supraventricular complexes, 602
- Supraventricular depolarization,
 echocardiogram, 603f
- Supraventricular ectopic beats, 610
- Supraventricular tachydysrhythmias, 610
- Surface oximetry, 137
- Surgical ablation of progressive ethmoid
 hematoma, 376-377
 complications of, 377
- Surgical excision of squamous cell
 carcinoma, 482
- Surgical forceps for cystic calculi, 833
- Surgical lasers, 394
- Surveillance, 25
- Susceptibility testing
 for eyelid lacerations, 464
 for foal pneumonia, 669
- Suspensory branch lesions in sport
 horses, 498-499
- Suspensory desmitis, extracorporeal
 shock wave therapy for, 565
- Suspensory ligaments
 body tearing, 499
 magnetic resonance imaging of, 509
 palpation of, 496
- Suture peritonitis complicating surgical
 ablation of progressive ethmoid
 hematoma, 377
- Swayback, 495
- Sweating in uterine torsion, 312
- Sweet clover causing hemorrhagic
 diathesis, 354
- Sweet feed, avoidance of, 810
- Sympathetic nerve, 101
- Sympathetic nervous system, effect on
 gastrointestinal motility, 109
- Syndrome X, 701
- Synovial degradation markers, 519
- Synovial fluid, biomarker sampling, 514
- Synovitis, idiopathic, atropine for, 557
- Synovium markers, 518
- Synovium synthesis markers, 519
- Synthetic colloid administration, 357
- Synthetic prostaglandin E2 (Cytosol), 98
- Systemic antibiotics, 460-461
- Systemic antiinflammatories, 460
- Systemic corticosteroids, 460
 for heaves, 418
- Systemic inflammatory response
 syndromes (SIRS), 167
- Systemic lupus erythematosus (SLIE), 177
- Systemic nonsteroidal antiinflammatory
 drugs (NSAIDs), 460
 potency of, 460t
- Systemic therapy, 460-461
- Systolic murmurs, echocardiogram
 indications for, 614b
- ## T
- T3. *See* T3 (triiodothyronine)
- T3 (triiodothyronine) test, 250
- T wave, 576
- TA. *See* Tracheal aspirates (TA)
- Tabanids, 46, 191
- Tabanus*, 186
- Tachyarrhythmia-induced
 cardiomyopathy, 596
- Tachydysrhythmias, 610-611
- Tachypnea, 401
- Tack, proper fit of, 570
- Tagamet. *See* Cimetidine (Tagamet)
- Tail, paralysis of, 755
- Tall teeth, 85, 85f
- Talus lysis, cysts of, computed
 tomography of, 507
- Tampon for vaginal adhesions, 327

- Tansy ragwort, 789
 Tapetum lucidum, 454-455
 Tapeworm, 138
 Tapeworm eggs
 detection of, 158-159
 microscopic appearance of, 159f
Taraxacum officinal, 761
 Tarsocrural joint effusion, 496
 Tarsus, cysts of, computed tomography of, 507
 Tartar shampoo, 199
 Tartrate-resistant acid phosphatase (TRAP), 518
 Tasometatarsal joints, osteoarthritis, extracorporeal shock wave therapy for, 565
Taylorella equigenitalis, 229
 TBA. *See* Tracheobronchial aspirate (TBA)
 TCDD. *See* Tetrachlorodibenzodioxin (TCDD)
 Tc99m. *See* Technetium 99m (Tc99m)
 TDM. *See* Therapeutic drug monitoring (TDM)
 Tear film
 distribution, 489
 elimination of, 489
 leukocytes blocking ocular infection, 477
 opacity of, 450
 production of, 488-489
 Tearing, 478
 Tears
 distribution of, 491
 insufficiency of, 466
 lysozymes in blocking ocular infection, 477
 measurement of, 491
 Technetium 99m (Tc99m), 500
 99m technetium methylene diphosphonate (99mTc-MDP), 371-372
 Teeth
 eruption of, 373-374
 nomenclature of, 83f
 Tegagel, 223
 Telazol, 18
 Telemetric ECG recorders, 577
 Telemetric ECGs, 602
 Telencephalon, 764
 Tellington-Jones, Linda, 570
 Teloepitides, 518
 Temperature affecting spermatozoa, 266
 Temperature control for interstitial pneumonia, 428
 Temporal bulbar conjunctiva, 452
 Temporary tarsorrhaphy, 464
 Temporohyoid osteoarthropathy, 774
 Temporomandibular joints, palpation of, 495
 Tendinitis of superficial digital flexor, 499
 Tendon injuries, postoperative management of, 546
 Teniae, anatomy and physiology of, 138
 Tennessee Walking Horses, glaucoma in, 486
 Tenosynovitis, 496
 Tenotomy scissors, 460
 TENS. *See* Transcutaneous electrical nerve stimulation (TENS)
 Teratoma
 of ovaries, 262, 263f
 of testicles, 308
 Terbutaline sulfate (Bricanyl), 817, 817f
 for heaves, 419
 Term mare, torsion in, 313
 Test strip kits, 316
 Testicles
 atrophy of, 308
 biopsy of in subfertile stallions, 259-260
 hypoplasia of, 308
 lesions of, 308-309
 neoplasms of, 308
 temperature of, 306
 torsion of, 308-309
 surgery of, 309f
 Testosterone, 257
 during pregnancy, 261
 for inadequate libido, 318
 in subfertile stallions
 diagnostic measurement of, 258
 temporal changes in, 259f, 260f
 with granulosa cell tumors, 262-263
 Tetanus, 775
 Tetanus prophylaxis
 for abdominal laparoscopy, 149
 for perineal lacerations, 333
 Tetanus toxoid for eyelid lacerations, 465
 Tetrachlorodibenzodioxin (TCDD), 90
 Tetracyclines, 6
 avoidance of, 745
 dosage optimization of, 9
 for equine monocytic Ehrlichiosis, 77
 for Lyme disease, 54
 for neonates, 4
 Tetrahydropyrimidines, cyathostomiasis resistance to, 162
 Tetralogy of Fallot, 358, 599-600, 599f
 Thalamus, 764
 Theca cells, 261
Theileria equi, 347
 Theiler's disease, 170, 172
Thelazia, 194, 474
 Theophylline for interstitial pneumonia, 428
 Therapeutic drug monitoring (TDM), 852
 Therapeutic index, 457
 Therapeutic lasers, 394
 Therapeutic shoeing
 for digital flexor apparatus contracture, 534
 for insufficient support of bony column, 535
 for laminitis, 522
 Therapeutic trailer ride for gas colic, 115
 Thermal burns, 220
 of cornea, 466
 Thermal injury to cornea, 466
 Thermal pattern, 503
 Thermograms, production of, 503-504
 Thermographic camera, purchase of, 502-503
 Thermography, 502-504
 instrumentation for, 502-503
 instruments for, Internet addresses for, 503t
 physiology of, 503
 relationship to other imaging modalities, 504
 uses of, 504
Thermoposis Montana, 782, 783f
 Thermoregulation, erythromycin interfering with, 676
 Thiabendazole
 for guttural pouch mycosis, 389
 for skin parasites, 196
 Thiamine
 for perinatal asphyxia syndrome, 647
 in parenteral nutrition, 113
 Thin-layer chromatography (TLC) in drug testing, 32-33
 Thiobarbiturates, 18
 Thiopental, 18
 Third carpal bone disease, computed tomography of, 506f
 Third heart sound (S3), 575
 Third metacarpal bone
 computed tomography of, 506f
 radiography of, 497
 Third metacarpal bones, radiography of, 498
 Third metacarpal lesions, computed tomography of, 506
 Third-degree atrioventricular block, 605
 Third-degree burns, 220
 Thoracic auscultation to differentiate trauma from pneumonia, 433
 Thoracic cavity air suction for pneumothorax, 434-435
 Thoracic compressions
 cessation of
 in cardiopulmonary resuscitation of foals, 654
 in foals, 652
 Thoracic radiographs, 434, 435
 Thoracic trauma, clinical signs of, 433
 Thoracic ultrasonography of pleuropneumonia, 421-423
 Thoracolumbar spinal cord disorders, 753-755
 Thoracolumbar spinal pain, 496
 Thoracostomy for pleural effusion drainage, 423
 Thorax, trauma to, 433
 Thoroughbred horses
 arytenoid chondrosis in, 381
 atrioventricular block
 postexercise electrocardiogram, 605f
 axial deviation of the aryepiglottic folds in, 379
 cervical stenotic myelopathy in, 747
 epistaxis in, incidence of, 430
 exercise-induced pulmonary hemorrhage in, 429
 post mortem examination of, 430
 with epistaxis, 429-430
 glaucoma in, 486
 hemophilia A in, 351
 lesions in, 498
 on treadmill, base-apex
 electrocardiogram of, 586f
 packed cell volume of, 337
 prepurchase examination of, 493
 recurrent exertional rhabdomyolysis in, 728
 respiratory sinus arrhythmia, ambulatory echocardiography, 605f
 resting base-apex ECG from, 578f
 sarcoïd in, 204, 484
 twin ovulation, incidence of, 245
 typical bacterial pathogens in, 414
 with atopy, 181
 with rhabdomyolysis, 733
 Threadleaf groundsel, 789
 Three-dimensional shock wave field, 562
 Three-pulse gonadotropin-releasing hormone challenge test, 259
 Thrombocytopenia, 349-350
 diagnosis of, 360
 Thromboembolic colic, 626
 Thromboembolic colic, diagnosis of, 627
 Thromboembolism, 626-627

- Thrombolytic therapy for jugular vein thrombophlebitis, 626
- Thrombophlebitis of jugular veins, 384
- Thrombosis of jugular veins, 384
- Thrombosis with equine viral arteritis, 363-364
- Thrombus, maxillary vein, ultrasound, 626f
- Thrusting, difficulties with, 318
- Thyroid dysfunction, 805-806
- Thyroid function
- and fertility, 250-251
 - diagnosis of, 250-251
 - testing of, indications for, 251
- Thyroid hormone assays, cost of, 251
- Thyroid hormone supplementation, 806
- Thyroid-stimulating hormone, 250
- Thyrotropin, 805
- Thyrotropin stimulation test with pituitary pars intermedia dysfunction, 809
- Thyrotropin-releasing hormone (TRH), 805
- Thyroxine supplementation, 251
- Tibial nerve, damage to, 735
- Tibial tarsal joint, osteochondritis dissecans in, 499
- Tibia-tailhead triangle, male fetus, 293
- Ticarcillin
- in NFDSM-G extender formulation, 267
- Ticarcillin for neonatal septicemia, 661t
- Ticarcillin-clavulanate for neonatal septicemia, 4
- Tick paralysis, 740
- differentiation of, 743t
- Ticks, 54, 188t, 189
- ear infestations with, 189
- Tidal volume, 437
- in foals, 687-688
- Tilade. *See* Nedocromil sodium (Tilade)
- Tilmicosin, 10
- Timing of heart murmurs, 576
- Timolol maleate (Timoptic), 487
- Timoptic. *See* Timolol maleate (Timoptic)
- TIMPs. *See* Tissue inhibitor of metalloproteinases (TIMPs)
- Tissue inhibitor of metalloproteinases (TIMPs), 517
- Tissue selenium, 803
- Titret, 316
- TLC. *See* Thin-layer chromatography (TLC)
- TLEAF. *See* Transendoscopic laser excision of the aryepiglottic folds (TLEAF)
- TMS. *See* Trimethoprim-sulfonamide (TMS)
- TNCC. *See* Total nucleated cell counts (TNCC)
- TNF-alpha. *See* Tumor necrosis factor-alpha (TNF-alpha)
- Tobramycin for ocular emergencies, 463t
- Tocolytics
- for fetal compromise, 632
 - for placental hydrops, 302
 - for placentitis, 300
- Alpha-tocopherol (Vitamin E), 744
- deficiency of, 620
 - for anhidrosis, 817
 - for cervical stenotic myelopathy, 748
 - for chronic nonsuppurative inflammatory hepatitis management, 173
 - for EMND, 745, 753
 - for equine degenerative myeloencephalopathy in, 749
- Alpha-tocopherol (Vitamin E)—cont'd
- for equine protozoal myelitis, 754
 - for exertional rhabdomyolysis, 730
 - for perinatal asphyxia syndrome, 647, 648t
 - in parenteral nutrition, 113
- Toewalking, 493
- Toilettage, 408
- Tolerance, definition of, 162
- Toluidine blue stain, 416
- Tom Cat catheter, 491
- Tomato bugs, 784
- Tongue, lymphoma of, 360
- Tonopen applanation tonometer, 486
- TonoPen XL, 462
- Topical antibiotics
- formulation of, 458t
 - penetration of, 461b
- Topical corticosteroids for ocular emergencies, 464
- Topical dyes, 451
- Topical ocular drugs, 458-459, 458b, 475
- Topical treatment, 457-459
- Total nucleated cell counts (TNCC) in tracheal aspirates, 404
- Total parenteral nutrition for duodenitis-proximal jejunitis, 123
- Total protein concentration (TPr), 295
- Toxic mares, 332
- Toxic conditions causing interstitial pneumonia, 427
- Toxic epidermal necrolysis, 177
- Toxic line, 105
- Toxin-induced laminitis, 787
- Toxoplasmosis, 469
- TPr. *See* Total protein concentration (TPr)
- Trabecular ventricular septal defects (VSD), 598
- Trace mineral supplementation, 779
- Tracheal aspirates (TA), 401-406
- and subclinical disease, 406
 - cytology of, 404-405
 - indications for, 401-402
 - interpretation of, 403-404
 - microbial culture in, 406
 - sample handling, 403
 - slide preparation and staining for, 403
 - technique for, 402-403
 - transportation before, 403
 - vs. bronchoalveolar lavage, 401-402
- Tracheobronchial aspirate (TBA) for foal pneumonia, 669
- for *Rhodococcus equi* infections, 61
- Tracheostomy for myasthenia, 745
- Tracheotomy for arytenoid chondrosis, 382
- Traction devices, 530
- Training techniques, 570
- Tranexamic acid (Cyklokapron) for acute blood loss, 341
- Tranquilizers, 17-18
- for ocular emergencies, 464t
 - for penile paralysis, 304
 - for postpartum hemorrhage, 330
- Transabdominal imaging for fetal compromise, 632
- Transabdominal ultrasonography
- determining abdominocentesis sites, 155
 - in uterine torsion, 312
 - of liver, 170
 - of placenta, 298
- Transabdominal ultrasound-guided fetal cardiac puncture, 247-248
- Transcervical uterine lavage, 280, 281f
- Transcutaneous electrical nerve stimulation (TENS), 569
- Transendoscopic laser excision of the aryepiglottic folds (TLEAF), 379-380
- Transfusion volume, determination of, 639
- Transient hypogammaglobulinemia in foals, 695
- Transilluminator for fundus examination, 453-454
- Transportation
- before tracheal aspirates, 403
 - of sick neonatal foal, 635
- Transported cooled semen, factors influencing success rates with, 266
- Transposition of the great vessels, 594
- Transrectal imaging for fetal compromise, 632
- Transrectal ultrasonography
- and retained fetal membranes, 331
 - for placental hydrops, 301
 - of placenta, 298-299
 - prior to endometrial sampling, 229
 - with reproduction probe, 155
- Transtacheal aspiration (TTA)
- endoscopic technique for, 402-403
 - with guarded catheters, 402-403
 - with unguarded catheters, 402
 - inflammation in, 413
- Transvaginal adhesions, 327
- Transvaginal reduction, flunixin meglumine for, 247
- Transvaginal ultrasound-guided allantocentesis, 247
- Transvaginal ultrasound-guided follicular aspirations for oocyte collection, 286
- Transvenous pacemaker for dysrhythmias, 605
- Transverse presentation, 321-322
- Transverse ridges, 86
- TRAP. *See* Tartrate-resistant acid phosphatase (TRAP)
- Trauma
- and cervical stenotic myelopathy, 747
 - associated with signs of forebrain disease, 765
- Traumatic splenic rupture, 340
- Treadmill, 413
- of FLAIR strips, 432
- Trental. *See* Pentoxifylline (Trental)
- Trephine site, sinuses, 372f
- TRH. *See* Thyrotropin-releasing hormone (TRH)
- Triamcinolone
- for cutaneous habronemiasis, 196
 - for equine recurrent uveitis, 471t
- Triamcinolone acetate for idiopathic synovitis, 557
- Triamcinolone acetonide
- equine studies of, 552-553
 - for collagenolytic granuloma, 207
 - for cutaneous lymphosarcoma, 210
 - for heaves, 418
- Triamcinolone acetonide (Vetalog), 552
- Triamcinolone hexacetonide, 552
- Trichlorfon
- for cutaneous habronemiasis, 305
 - for skin parasites, 196
- Trichlormethiazide-dexamethasone (Naquasone), 16
- Trichodesma*, 426
- Trichophyton*, 199

- Trichophyton dermatophytosis*, 218
Trichophyton equinum, 199, 201
Trichophyton verrucosum, 199
Trichosporon, 792
 Tricuspid atresia, 600-601
 Tricuspid endocarditis with septic jugular vein thrombophlebitis, 614
 Tricuspid prolapse, murmurs of, 613
 Tricuspid regurgitation, 574, 613-614
 two-dimensional echocardiography, 614f
 Tricuspid valve atresia, 594
 Trifoliosis, 790
Trifolium hybridum poisoning, 790-791
Trifolium pratense poisoning, 790-791
 Trigeminal nerve dysfunction, 476
 Trigger points, 569
 Trimethoprim
 for pleuropneumonia, 424
 neonatal metabolism of, 3
 Trimethoprim sulfa
 for neonatal septicemia, 658, 660
 for pregnant mares, 231
 for retained fetal membranes, 332
 Trimethoprim-sulfadiazine for cystitis, 759
 Trimethoprim-sulfamethoxazole
 for guttural pouch empyema, 387
 for ocular emergencies, 463t
 Trimethoprim-sulfamethoxazole for respiratory disease, 39
 Trimethoprim-sulfonamide for rectal tears, 152
 Trimethoprim-sulfonamide (TMS), 6
 for acute respiratory distress syndrome, 676
 for cystitis, 838
 for foal pneumonia, 671
 for neonatal septicemia, 4, 661t
 for *Rhodococcus equi* infections, 62
 for staphylococcal bacterial folliculitis, 198
 for strangles, 67
 Triple Block for upward fixation of the patella, 536
 Triple drip, 19
 Trocar needle, 459
 Trochlea, osteochondrosis dissecans of, 499
 Trochlear ridge, fat-suppressed sagittal image of, 511f
Trombicula, 188
Trombicula autumnalis, 188
 Trombiculidosis, 188
 Trombidiforms, 189
 Tropical horse tick, 189
 Tropicamide for posterior segment examination, 453
 Tru-cut biopsy device, 171
 Truss for penile trauma, 303
 TTA. *See* Transtracheal aspiration (TTA)
 TTEAM techniques, 570
 TTouch techniques, 570
 Tube casts for incomplete ossification of cuboidal bones, 664
 Tube feeding
 of neonatal foal, 633
 recommended schedule for, 709t
 Tuber sacrale, 496
 Tumor necrosis factor-alpha (TNF-alpha), 519
 Tunica albuginea
 hematoma within, 306
 tear in, 303
 Tunica flava abdominis, 310
 Turner's syndrome, 261
 T1-weighted (T1-wt), 509
 T2-weighted (T2-wt), 509
 Twin abortions, 245, 246f
 Twin fetuses, signs of, 632
 Twin ovulation, incidence of, 245
 Twin pregnancy causing retained fetal membranes, 330
 Twins, 245-248
 Twitch, 321
 during artificial insemination, 273
 for postpartum hemorrhage, 328
 Two Lead Arthroscopic Irrigation Set, 156
 Two-dimensional echocardiography, 578-579
 congestive heart failure, 615f
 for aortic cardiac fistulas, 625
 for ventral septal defects, 598
 pulmonary hypertension, 617f
 tricuspid regurgitation, 614f
 Two-layered closure for cesarean section, 322
 Tympany of colon, 132
 Type B toxoid, 800
 Type C toxoid, 800
 Type I procollagen propeptide, 518
 Type II collagen neoepitope, 516
 Type II procollagen propeptide, 517
 Type III procollagen propeptide, 519
 Tyzzer's disease, 170, 171
- U**
 Ubiquinone, 28-29
 Udder, development of in placentitis, 298
 UFA. *See* Upward fixation of the patella (UFA)
 Ulcerative keratitis, fungal infection
 associated with, 466
 Ulcerative keratomycosis, 466
 Ulcers, 22
 Ultrasonic nebulizers, 439
 for foal pneumonia, 672
 Ultrasonography
 of aortic aneurysms, 624
 of aortic cardiac fistulas, 625
 of cauda equina damage, 758
 of retinal detachment, 467
 of thromboembolism, 627
 of urinary tract, 823
 predicting ovulation, 242-245
 with thermography, 504
 Ultrasound
 follicular changes, 243-244
 for diaphragmatic hernia, 435
 for embryo transfers, 277
 for estrus staging, 242-245
 for fetal compromise, 632
 for fetal gender determination, 288
 for foal pneumonia, 669
 for fractured ribs, 436
 for pneumothorax, 434
 for postpartum hemorrhage, 328
 for small colon mesentery rupture, 325
 in neoplastic effusions, 424
 in premature foals, 634
 of exercise-induced pulmonary hemorrhage, 431
 of mare's reproductive tract, 272
 Ultraviolet light and squamous cell carcinoma in, 480
 Ultraviolet radiation, 174
 Umbilical cord, 297
 inspection of, 324
 Umbilical remnant infections, 658
 Umbilicus, 297
- UMN signs. *See* Upper motor neuron (UMN) signs
 Unassisted foaling, perineal lacerations during, 333
 Uncomplicated laryngeal hemiplegia vs. arytenoid chondrosis, 381-382
 Underbites, 86f, 87
 Unfractionated heparin therapy for laminitis, 108
 Ungual cartilages, 532
 Unilateral papular dermatosis, 207
 Unilocular granulosa cell tumors (GCT), ultrasonic image of, 262f
 Univentricular heart syndrome, 592f, 594
 Upper airway disease, 366-369
 equipment for, 366
 medical treatment of, 398-400
 resting horse
 examination of, 366-368
 Upper airway resistance and exercise-induced pulmonary hemorrhage, 432-433
 Upper eyelids, laceration of, 465
 Upper motor neuron (UMN) signs, 753-755
 Upper respiratory tract, laser surgery of, 393-396
 Upper urinary tract infections, 838
 Upside down foal, 320
 Upward fixation of the patella (UFA), 536-537
 Urachal disease, 857
 Ureteral defects, 828, 855f
 Ureterolithiasis, 832-833
 Urethra
 aerobic bacterial cultures of, 269
 calculi, 834
 defects, hematuria, 854-855
 pressure profiles, 824
 Urethritis, 837
 Urge incontinence, 824
 Urinalysis, 820-831, 846-847
 and chronic exertional rhabdomyolysis, 729
 with cauda equina damage, 758
 Urinary catheter, 492
 Urinary corticoid to creatinine ratio for pituitary pars intermedia dysfunction, 810
 Urinary incontinence, 824-826
 Urinary system
 examination of, 819-824
 hematology of, 820
 history of, 819
 physical examination of, 819
 serum biochemistry of, 820
 urinalysis, 820-831
 Urinary tract
 calculi of, 719-720
 congenital disorders of, 826-827
 disease of, 718-721
 endoscopy of, 822
 infection of, 837-839
 neoplasia of, 835-837
 neoplasms of, hematuria, 854
 nuclear scintigraphy of, 823
 obstructive disease of, 832-834
 radiography of, 823
 ultrasonography of, 823
 Urination in uterine torsion, 312
 Urine
 biomarker sampling, 514
 in semen, 255
 production of, 829
 increased, 843

- Urine fractional excretion values, 729f
 in cantharidin toxicosis, 785
 Urine samples for drug testing, 32
 Urine sediment, 821
 Urine specific gravity, 820, 841
 Uroabdomen, 681
 Urokinase for thromboembolism, 627
 Urolith, formation of, 832
 Urolithiasis
 clinical signs of, 832
 hematuria, 854
 Uroperitoneum, 326, 857-858
 Urticaria, 206
 histopathology of, 178
 Uterine artery
 rupture of, 327
 effect on peritoneal fluid, 296
 Uterine biopsy instrument, 376
 Uterine culture, 226-228
 Uterine culture instruments, 229
 Uterine culture swab, 226-227
 Uterine horns
 biopsy specimens from, 233
 intussusception of, 331
 ultrasound image of, 244f
 Uterine lavage, 227
 for retained fetal membranes, 332
 for uterine infection, 231
 Uterine lavage tube, 227
 Uterine prolapse, 325
 Uterine rupture, 301
 Uterine swab culture, 249
 Uterine torsion, 311-315
 cause of, 312f
 causing dystocia, 320
 complications of, 313
 correction of, 313-314
 diagnosis of, 312-313
 direction of, 312f
 effect on peritoneal fluid, 295
 fetal prognosis with, 314-315
 surgical correction of, 313-314
 Uteroplasenta, 632
 Uterus
 diagram of, 274f
 discharge from and retained fetal membranes, 331
 examination of for embryo transfers, 277
 inability to clear, 234
 inertia of causing retained fetal membranes, 330
 infection of causing dystocia, 320
 lavage of, 324
 placement of implant gun in, 284f
 rectal exam of, 331
 rupture of with uterine torsion, 313
 size of in after foaling mare, 249
 thickness of during late gestation, 299f
 ultrasound of, 244-245, 244f
 in recipient mares, 278
 Uvea, 466
 Uveitis
 causes of, 469t
 environmental triggers of, 470
 organisms associated with, 468
 recurrent episodes of, pathogenesis of, 469
- V**
- Vaccine
 for atopic dermatitis, 183
 for breeding stallions, 252
 for equine monocytic ehrlichiosis, 77
- Vaccine—cont'd
 for equine protozoal myeloencephalitis, 74
 for rabies, 770-771
 for uveitis, 470
 Neorickettsia risticii, 252
 Vagina
 effusions within, 306-307
 examination of in after foaling mare, 249
 lacerations of, 326-327
 Vaginal sac, distention of, 307f
 Vaginal speculum for endometrial swabs, 229
 Vaginal tunic, 306
 Vagolytic agents for dysrhythmias, 605
 Vagus nerve, 101
 Valgus deviations, 664-665
 Valley black gnat, 191
 Valvular heart disease, acquired, 613-619
 Vancomycin, 168
 Varus deviations, 664-665
 Vascular anomalies, 828
 Vascular diseases, 625-630
 Vascular phase of musculoskeletal nuclear scintigraphy, 500
 Vasculitis, 89, 363-365, 629-630
 clinical signs of, 364
 diagnosis of, 364
 etiology of, 363-364
 histopathology of, 179
 treatment of, 364-365, 476
 Vasoactive intestinal peptide (VIP) as neurotransmitter, 109
 Vasodilators for exercise-induced pulmonary hemorrhage, 432
 Vasopressin, 822
 in human cardiopulmonary resuscitation, 655
 Vectors, 24
 Vedaprofen (Quadrisol), 14
 for retained fetal membranes, 332
 VEE. *See* Venezuelan equine encephalitis (VEE)
 Vegetable oils, 708
 as concentrated energy source, 702
 supplements for colitis, 724
 Veins, temperature of, 503
 Venezuelan equine encephalitis (VEE), 48, 194, 766
 Ventilation, cessation of in cardiopulmonary resuscitation of foals, 654
 Ventilation imaging, 439
 Ventilation-perfusion pulmonary scintigraphy of thromboembolism, 627
 Ventipulmin. *See* Clenbuterol (Ventipulmin)
 Ventral atrial septum, 592f
 Ventral conchal sinus, 369
 Ventral midline approach for cesarean section, 322
 Ventral midline celiotomy
 for hernia, 307
 for uterine torsion, 314
 Ventral turbinates, examination of, 368
 Ventricular arrhythmias, 802
 Ventricular complexes, 602
 Ventricular depolarization, echocardiogram, 603f
 Ventricular ectopic beats, 610-611
 treatment of, 611
 Ventricular fibrillation, 612-613
- Ventricular premature contractions, 610
 electrocardiogram, 587f
 Ventricular premature depolarization (VPDs), 617-619
 in standing horse, electrocardiogram, 588f
 Ventricular pressures, digital recording of, 589
 Ventricular septal defects (VSD), 358, 592, 596-597
 echocardiography, 581f
 inlet, 596
 malalignment, 596
 outlet, 596
 paramembranous, 593f
 parasternal long axis reference view of, 584f
 pulmonary atresia with, 600
 subpulmonic, 596
 Ventricular septum, 592
 Ventricular tachycardia, 610
 ambulatory echocardiography, 612f
 electrocardiogram, 587f
 Ventricular tachydysrhythmias, 611-612
 Ventriculectomy, 385
 Ventriculocordectomy, 385
 Ventrotransverse presentation, 321-322
 Verminous arteritis, 128
 Verminous encephalitis, 767
 Verminous myelitis, 758
 Vernal transition period, 237
 physiologic events of, 238t
 Verrucous sarcoids, 203
 Vertebral abnormalities, nuclear scintigraphy of, 501
 Vertebral column, 755
 Vesicles, 217
 Vesicular stomatitis, 51-53, 88
 clinical signs of, 52
 diagnosis of, 52
 laboratory diagnosis of, 52-53
 pathogenesis of, 51
 prevention and control of, 53
 regulatory issues of, 51-52
 treatment of, 53
 Vesicular stomatitis virus (VSV), 51
 Vestibule, examination of in after foaling mare, 249
 Vet checks, 568
 Vetalog. *See* Triamcinolone acetonide (Vetalog)
 Veterinary Dynamics, 693
 Vetrax bandaging tape for foot, 547
 Vettec, 525
 Viborg's triangle, 68
Vicia villosa, 784
 Vicks, 319
 Vidarabine for herpetic keratitis, 475-476
 Video endoscopes, 366
 Video recording in preperformance testing, 499
 Vigro Complete Flush Solution, 280-281
 Villonodular synovitis, 498
 Vincristine for cutaneous lymphosarcoma, 211
 VIP. *See* Vasoactive intestinal peptide (VIP)
 Viral agents causing interstitial pneumonia, 425
 Viral encephalitis, 47-50
 prevention of, 770-771
 Viral encephalitis, 774
 Viral enteritis with gastroduodenal ulcer syndrome, 680
 Viral intestinal diarrhea in foals, 679-680